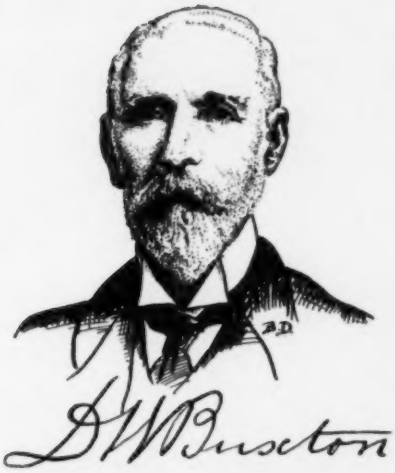


British Journal of Anaesthesia

JOINT EDITORS:
E. FALKNER HILL T CECIL GRAY
Editor of Postgraduate Educational Numbers R. P. HARBORD

Volume XXXII No. 6 June 1960

JOHN SHERRATT & SON : *Publishers*
ALTRINCHAM ENGLAND

At your service . . .

The finest apparatus covering all fields of anaesthesia is designed and manufactured by M.I.E.

Our expert knowledge is at all times at your disposal and is backed by a degree of service second to none.

Your requests will receive prompt attention.

Call, telephone or write

MEDICAL & INDUSTRIAL EQUIPMENT LTD.

SPECIALISTS IN ANAESTHETIC APPARATUS & SURGICAL INSTRUMENTS

10 & 12 NEW CAVENDISH STREET, LONDON W.1

Telephone : WELbeck 1851 and 1504 *Telegrams : Narcosis, Wesdo, London*

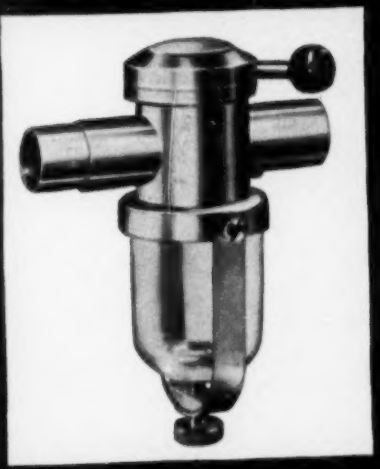
MANCHESTER, 152-154 Oxford Road
Phone : Ardwick 5906

TORONTO, CANADA, 83-85, Grenville Street
Phone : WALNUT 3-3845

British Oxygen Equipment and Gases...

THE GOLDMAN

halothane vaporiser



Primarily designed for the administration of halothane as an adjunct to nitrous oxide oxygen in dental surgery this compact vaporiser provides safe, flexible control of vapour concentration not only in dental anaesthesia but in open or closed circuit with Boyle type apparatus as well.

The Goldman vaporiser is so designed that under normal conditions of flow rate and fluid temperature the vapour output will not exceed 3%.

For illustrated literature please write to British Oxygen Gases Limited, Medical Division, Great West Road, Brentford, Middlesex.

...used every day to ease pain and save lives

Cyprane

specialise in

PRECISION ANAESTHETIC APPARATUS

The present standard products are as follows:—

- **CALIBRATED VAPORIZERS** for volatile anaesthetic agents.
  - FLUOTEC ... ... for "Fluothane" (standard range 0·5%—4·0%).
  - TRITEC ... ... for "Trilene" (standard range 0·5%—1·5%)
  - CHLOROTEC ... ... for Chloroform (standard range 0·5%—5·0%).
  - AZEOTEC ... ... for the azeotropic mixture of "Fluothane" with ether.
- **TECOTA MARK 6 INHALER** for analgesia set to give 0·5% Trilene in air and approved for use by Midwives.
- **THE CYPRANE INHALER** ... for "Trilene" analgesia in midwifery and minor surgery.
- **A.E. GAS-OXYGEN Apparatus** for the administration of nitrous oxide/oxygen (range 0—100%) in Dental and General anaesthesia.

Cyprane Limited

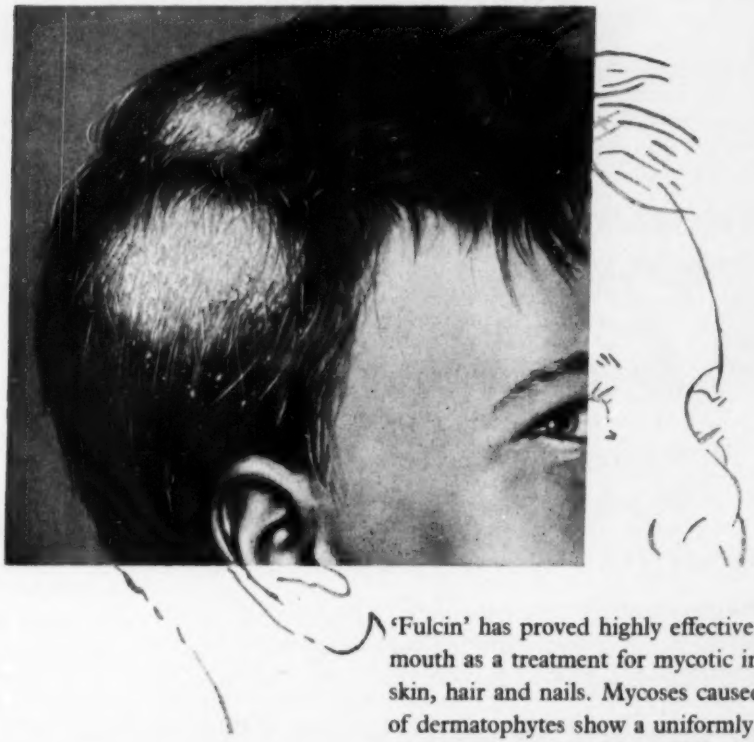
HAWORTH, KEIGHLEY, YORKSHIRE

(*Telephone:* Haworth 3286)

"Trilene" and "Fluothane" are the registered trade marks of Imperial Chemical Industries Ltd., and "Vinesthene" is that of May & Baker Ltd.

A revolutionary advance in the treatment of ringworm infections

A case of ringworm of the scalp, of the non-inflammatory type



Fulcin
TRADE MARK
GRISEOFULVIN

'Fulcin' has proved highly effective when given by mouth as a treatment for mycotic infections of the skin, hair and nails. Mycoses caused by various species of dermatophytes show a uniformly favourable response. The drug is well tolerated and only minor side effects may be observed in a few patients. These side effects are usually transient and, in most cases, disappear during treatment. *A daily dose of* 1 *gramme* (1 *'Fulcin' tablet four times a day*) *is adequate for most cases.*

Packings. Scored tablets 250 mg. each.
Containers of 100 and 1,000. Basic N.H.S. cost of treatment is 2/5d. per day. 100 tablets, 60/-

Literature and further information available on request.

IMPERIAL CHEMICAL INDUSTRIES LIMITED PHARMACEUTICALS DIVISION WILMSLOW CHESHIRE

Ph.24

The new potent ANALEPTIC

Vandid

(VANILLIC ACID DIETHYLAMIDE)

. . . increases the frequency and depth of respiration in seconds

MORE POTENT THAN OTHER ANALEPTICS

In animal studies, 'Vandid' was found to be four times more effective than leptazol and fifteen times more effective than nikethamide as a respiratory stimulant. (*Wein Z. inn. Med.*, 1952, 1 : 16)

MORE EFFECTIVE IN BARBITURATE OVERDOSAGE

". . . As a respiratory stimulant bemegride has repeatedly failed . . . In fact as a respiratory stimulant it would appear to be much less effective than the convulsant vanillic acid diethylamide".

(*Brit. med. J.*, 1959, 2 : 1332)

VANDID IS SAFE . . . . DOSAGE IS SIMPLE . . . .

Within the recommended dosage range (1-2 ml) toxic reactions are rarely seen.

'Vandid' is a trade mark

RIKER

BASIC N.H.S. PRICES
ampoules (5% solution)
6 x 2 ml 13/-
6 x 5 ml 18/-

RIKER LABORATORIES LIMITED, Loughborough, Leicestershire

60/2-VI

NOTICE TO CONTRIBUTORS

This Journal is for the publication of original work in all branches of anaesthesia, including the application of basic sciences. The March and September issues deal mainly with material of educational value.

Papers. Papers are accepted on the understanding that they have not been and will not be published in whole or in part in any other journal. They are subject to editorial revision. Manuscripts should indicate the title of the paper, the name, qualifications and full address of the author, and be in double-spaced typing on one side only of quarto paper with a wide margin.

Abbreviations, Weights and Measures. Abbreviations should follow the convention adopted by the *Journal of Physiology*. Weights and measures, dosages, etc., should be expressed in the metric system.

Tables. All tables should be on separate sheets and be capable of interpretation without reference to the text.

Illustrations. Photographs should be unmounted, glossy prints. Drawings, charts and graphs should be in black indian ink on white paper. All illustrations should be clearly numbered with reference to the text on the back and should be accompanied by a suitable legend. The name of the author and title of the paper should also be written on the back of the illustrations.

References. There should be a table of references at the conclusion of the paper. These references should be arranged according to the Harvard system and in alphabetical order. Abbreviations in the references should be according to the World List of Scientific Publications.

In the Harvard system, in the text the year of publication must follow the author's name, more than one paper in any one year being indicated by a small letter (a, b, c) after the date. In the references, the order should be: author's name, followed by initials; year of publication in parentheses; title of paper to which reference is made; title of publication underlined with a single line (to indicate italics) and abbreviated in accordance with the World List of Scientific Periodicals; volume number in arabic numerals, underlined with a wavy line (to indicate bold face); the number of the first page in arabic numerals; thus: Howell, T. H., Harth, J. A. P., and Dietrich, M. (1954). The Use of Chlorpromazine in Geriatrics. *Practitioner*, **173**, 172.

In the case of books, the reference should be as follows: name of author and initials; year of publication in parentheses; title of the book; number of edition; page number; town of origin, publisher; e.g., Hewer, C. L. (1948). *Recent Advances in Anaesthesia and Analgesia*, 6th ed., p. 120, London: Churchill.

The *British Journal of Anaesthesia* should be referred to in the references as *Brit. J. Anaesth.*

Proofs. Proofs will be sent to all contributors. These should be corrected and returned to the Joint Editors within forty-eight hours.

Reprints. Twenty-five reprints of articles will be dispatched to the authors after publication. Further reprints can be supplied if application is made when the proofs are returned.

Copyright. Papers which have been published become the property of the Journal and permission to republish must be obtained from the Editors.

Short and long relaxation

TASTES VARY, AND SO DO REQUIREMENTS. THE SYNTHETIC MUSCLE RELAXANTS IN THE RANGE OF **M&B** BRAND MEDICAL PRODUCTS MEET NEEDS AS DIVERSE AS PROLONGED MAJOR SURGERY AND ELECTRO CONVULSIVE THERAPY.

* ideal for procedures of all but the shortest duration
* completely reversed by neostigmine
* does not cause significant release of histamine

'FLAXEDIL'
trade mark brand
GALLAMINE TRIETHIODIDE INJECTION B.P.

* for short procedures (3 to 5 minutes) suitable for endoscopies, intubation, and orthopaedic manipulations

'BREVIDIL' M
trade mark brand
SUXAMETHONIUM BROMIDE

* extremely short duration of action (2 to 4 minutes) with marked freedom from post-operative pain
* suitable for all brief procedures including dental surgery.

'BREVIDIL' E
trade mark brand
SUXETHONIUM BROMIDE

MANUFACTURED BY MAY & BAKER LTD

M&B brand Medical Products

DISTRIBUTORS

PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD

DAGENHAM

ALLEN & HANBURYS LTD

introduce

THE SEALEY Portable

DEFIBRILLATOR

MODEL
P.D.2

—ready for immediate use
in cardiac emergencies

DESCRIPTIVE LITERATURE AVAILABLE ON REQUEST

NOTE: This Portable Defibrillator is only one of a comprehensive range of Sealey Electrical Cardiac Resuscitation Apparatus, including internal and external defibrillators and cardiac pacemakers.

SOLE WORLD DISTRIBUTORS

ALLEN & HANBURYS LTD *(SURGICAL DIVISION)* LONDON E2

THE INTERNATIONAL MEDICAL ABSTRACTING SERVICE

EXCERPTA MEDICA

AMSTERDAM — NEW YORK

offers to medical science:

For each medical specialty a MONTHLY ABSTRACTING JOURNAL containing abstracts in English from every available medical journal in the world.

Two special publications:

(1) SIDE EFFECTS OF DRUGS: an exhaustive and up-to-date review of the use of present-day drugs and their side effects, edited and compiled by L. Meyler, M.D.

(2) PHARMACOLOGICAL AND CHEMICAL SYNONYMS: a collection of more than 8,000 references from the medical literature of the world, compiled by E. E. J. Marler, M.D., M.Sc., Ph.D.

A TRANSLATION SERVICE for the rapid translation of medical publications and manuscripts.

Address your requests to our sole distributors for Great Britain and the Commonwealth (excluding Canada and South Africa)

E. & S. LIVINGSTONE, LTD. *Teviot Place, Edinburgh, 1*

BOARD OF MANAGEMENT AND PROPRIETORS

General Editors

E. FALKNER HILL, *Late Senior Anaesthetist, Manchester Royal Infirmary*

T. CECIL GRAY, *Professor of Anaesthesia, University of Liverpool*

Editor of Postgraduate Educational Numbers

R. P. HARBORD, *Reader in Anaesthetics, University of Leeds*

Consultant Editors

J. W. DUNDEE, *Senior Lecturer in Anaesthetics, Queen's University of Belfast, Northern Ireland.*

H. H. PINKERTON, *Joint Lecturer in Anaesthetics, University of Glasgow, Scotland*

W. W. MUSHIN, *Professor of Anaesthetics, Welsh National School of Medicine, Wales*

R. F. WOOLMER, *Professor of Anaesthetics, Department of Anaesthesia, Royal College of Surgeons of England, London*

Assistant Editors

A. R. HUNTER, *Consultant Anaesthetist, Manchester Royal Infirmary*

J. E. RIDING, *Demonstrator to the Department of Anaesthesia, University of Liverpool*

M. H. ARMSTRONG DAVISON, *Consultant Anaesthetist, The United Newcastle upon Tyne Teaching Hospitals*
R. C. LAWRENCE, *Consultant Anaesthetist, United Leeds Hospitals.*
T. J. C. MACDONALD, *Consultant Anaesthetist, Aberdeen Royal Infirmary*
A. G. MILLER, *Consultant Anaesthetist, Western Infirmary, Glasgow*
R. J. MINNITT, *Senior Honorary Anaesthetist, Royal Liverpool United Hospitals*
R. E. PLEASANCE, *Lecturer in Anaesthetics, University of Sheffield*
H. Q. O. WHEELER, *Consultant Anaesthetist, Department of Neurological Surgery, General Hospital, Sunderland.*
W. D. WYLIE, *Consultant Anaesthetist, St. Thomas's Hospital, London*

Papers for publication and all editorial communications should be addressed to either of the Editors at 48–50 Bedford Street North, Liverpool, 7. Business communications should be addressed to the publishers: JOHN SHERRATT AND SON, Park Road, Altrincham, Cheshire.

Published monthly. Annual subscription (post free): Inland £3 15*s.*; Overseas £4 4*s.*; United States and South Americas $12.00.

© John Sherratt and Son, 1959.

Further progress in Hospital Instruments

BURNDEPT BE.277

BODY PULSE METER

Battery operated (truly portable)—sensitive—reliable and simple to use. Inexpensive.

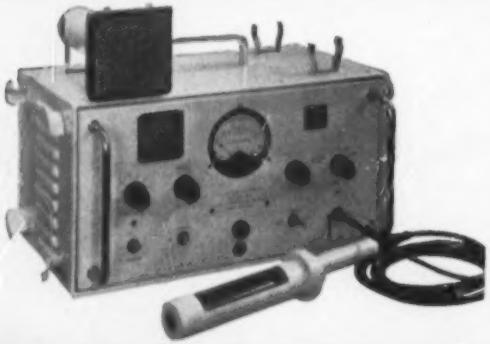
Brief specification:
Visual Indication of Arterial Pulsation. A Microphone acting as a transducer, applied to the pulp of the terminal phalanx of any digit is used to operate the meter which thus indicates the arterial pulsations.
In conjunction with a sphygmomanometer it can be used to measure systolic blood pressure, the BE. 277 taking the place of the stethoscope.

BURNDEPT BN.120

Universal Scintillation Counter

A truly adaptable instrument which allows for several types of Collimators, different grades and types of Crystals, thus making it a multi-purpose Scintillation Counter.
A Cathode Follower and Head Amplifier are available, designed to be truly compatible, comprising:

Lead Skirt BN 125 Wide Angle Collimator BN 122
Narrow Angle Collimator Attachment BN 124
Slotted Collimator BN 126 Adjustable Clamp BN 121
Adjustable Clamp BN 123 Cathode Follower Unit BN 127
Connectors



BURNDEPT BN.110 (AERE Cat. No. 3-7/15544)

General Purpose Ratemeter Mk. II

Associated Probes: Alpha—BN. 111.
Beta/Gamma—BN. 108.

Brief Specification: Designed primarily for measuring the radiation from contaminated surfaces.
Two probes are used for the detection of radiation.
A Large Area Alpha Probe BN. 111 operating on the scintillation counter principle.
A Beta/Gamma Probe BN. 108 using a thin walled Geiger tube.
Ranges of 0-5, 0-50, 0-500 and 0-5000 counts/sec.

BURNDEPT BN.106

Head Amplifier—(for use with BN. 110 & BN. 120).

Brief specification: A wide band linear amplifier for amplifying pulses having a short development time.
Small and compact and very suitable for use between scintillation counter or ion chambers and ratemeters or scalers.

Enquiries to: CONTRACT SALES DEPT., BURNDEPT LIMITED, ERITH, KENT. Telephone: Erith 33080

" *I would have everie man write what he knowes and no more.*"—MONTAIGNE

BRITISH JOURNAL OF ANAESTHESIA

VOL. XXXII, No. 6 JUNE 1960

EDITORIAL

MINOR SEQUELAE OF ANAESTHESIA

WE published in the May issue of this Journal a paper (*Brit. J. Anaesth.*, **32**, 219) by Drs. Conway, Miller and Sugden on "Sore Throat after Anaesthesia," which showed that one quarter of all the patients under review suffered from this disagreeable result of anaesthesia. Of the patients who were intubated, nearly two out of every five were so afflicted, and in summary it would seem that something like one out of every five of our patients is likely to be afflicted with a severe sore throat after anaesthesia. This is only one of the comparatively minor sequelae of our ministrations and some of these are, with a little extra care, preventable. In regard to sore throat, it is the clinical impression of at least one department that careful attention to the sterility of tubes and suction catheters and the use of a practically non-touch technique for their introduction seems to reduce the incidence.

There are other minor sequelae, the incidence of which we may also tend to take too much for granted. How many patients wake up to find legs or/and arms afflicted by the haematomata which are regarded by many anaesthetists as almost among the necessary evils attendant upon modern anaesthesia. "How necessary" is, at least, debatable. Again, quite a percentage of the population of this country must by now have been afflicted with post-suxamethonium pains. One well-known teacher was recently heard to say that, although he believed a small dose of nondepolarizing relaxant given before suxamethonium would reduce the incidence of this complication, yet "somehow or other" this was not the usual procedure even in the units in which he worked. These pains can be very crippling and in at least one instance have almost led to litigation. We suggest that they should not be regarded lightly and that every possible effort should be made to reduce their incidence, including a less light-hearted use of suxamethonium where it is not obviously indicated.

In conclusion, while there is proceeding a great deal of investigation into more refined methods of suspended animation (which are only likely to be applied to a very small proportion of the population) surely there is a greater need for more effort to be devoted towards the reduction in incidences of some of these minor sequelae. It would seem that the first step is for the administrators of anaesthesia to be aware of their importance and to exercise ever greater care to avoid them.

Brit. J. Anaesth. (1960), **32**, 248

STUDIES WITH AN ORGANIC BUFFER (T.H.A.M.) DURING APNOEIC OXYGENATION IN DOGS

BY

R. A. MILLAR, G. F. BRINDLE AND R. G. B. GILBERT

Department of Anaesthesia, Montreal Neurological Institute and McGill University, Montreal, P.Q., Canada

RECENT studies, using the condition of apnoeic oxygenation ("diffusion respiration") as a means of inducing progressive carbon dioxide accumulation (Draper, Whitehead and Spencer, 1947; Holmdahl, 1956), showed that plasma levels of adrenaline and noradrenaline were raised during acute respiratory acidosis. Average findings, after 1 hour of apnoeic oxygenation, were an arterial pH of 6.55, a P_{CO_2} of 338 mm Hg, and a total plasma catecholamine level of 24 μg/l. (Millar, 1960).

An organic buffer, tris-(hydroxymethyl) aminomethane (T.H.A.M.), was shown by Nahas and Rosen (1959) to be effective in reducing or preventing the extreme pH changes which accompany apnoeic oxygenation. In view of Nahas' findings our previous studies have been extended, mainly to determine acid-base balance and plasma catecholamine levels during buffered apnoeic oxygenation in dogs; the results, and some other effects of T.H.A.M., will be presented and discussed here.

METHOD

Nine experiments were performed, the conditions resembling closely those employed in an earlier study (Millar, 1960). After induction of light anaesthesia with thiopentone, dogs were allowed to breathe 100 per cent oxygen through a No. 10 cuffed Magill tube for approximately 20 minutes, while one femoral artery was cannulated for withdrawal of blood samples and recording of blood pressure. A slow continuous infusion of suxamethonium chloride (0.2 per cent) was started, and the animals were ventilated with 100 per cent oxygen for a further 10 minutes, during which control blood samples were withdrawn. They were then left in a state of apnoeic oxygenation, the endotracheal tube being connected, through a T-piece with a slack expiratory valve, to a 5-litre bag which was kept loosely filled with a slow flow of 100 per cent oxygen.

T.H.A.M. was supplied as an anhydrous, lyophilized sterile powder containing tris-(hydroxymethyl) amino-methane 36.3 g., with sodium chloride 1.75 g. and potassium chloride 0.37 g. To this was added 1,000 or 500 ml distilled water to give the 0.33M. or 0.66M. solution of pH 10.6.

The recommended 0.33M. solution was given by intravenous infusion in the first two experiments but, because of the large volumes required to buffer adequately the severe respiratory acidosis induced by apnoeic oxygenation, the more convenient 0.66M. solution was used subsequently. Infusion rates of 0.5–1 ml/kg/min were employed. In some experiments T.H.A.M. was administered at the start of the period of apnoea and later discontinued; in other studies it was given after apnoea had already lasted for 1 hour or longer.

Arterial blood samples were taken at variable times before, during and after administration of T.H.A.M. Immediately after each blood sample was withdrawn, an equal volume of normal saline was injected intravenously, to prevent or retard any rise in plasma adrenaline which might result from blood sampling.

Blood for pH, P_{CO_2} and "standard" bicarbonate estimations (8 ml) was withdrawn anaerobically into syringes moistened with heparin solution. Whole blood pH and the pH of separated plasma, equilibrated at 38°C with a known P_{CO_2} tension (40 mm Hg), were determined at once, using the "Radiometer" pH meter and Astrup apparatus (Astrup and Schroder, 1956);

from these two pH determinations the "standard" bicarbonate in separated plasma (at a P_{CO_2} of 40 mm Hg) and the P_{CO_2} were calculated as described by Astrup (1956). Because of the extreme increase in bicarbonate produced by infusion of T.H.A.M. during respiratory acidosis, the available graphs relating equilibrated plasma pH with the "standard" bicarbonate and P_{CO_2} were sometimes incomplete; in such instances the "standard" bicarbonate is given as (>50) and the estimated P_{CO_2} value is tabulated in brackets to indicate that the figure is approximate.

Blood samples for assay of adrenaline and noradrenaline (35 ml) were withdrawn into glass tubes containing a few drops of heparin solution (10,000 units/ml) and were centrifuged immediately. The plasma was aspirated, filtered and applied to alumina columns. Adrenaline and noradrenaline in the plasma eluates were estimated fluorimetrically by the trihydroxyindole method which has been described previously (Millar, Keener and Benfey, 1959). An additional step was introduced into the method after development of fluorescence, 0.5 ml of 1 per cent disodium ethylenediamine tetra-acetate being added to the final mixture prior to measurement in the photofluorimeter. Although slightly reducing recovery, this ensures consistently low "blank" values. An error of ±25 per cent is involved in the differential estimation of adrenaline and noradrenaline in single plasma samples and the values, which refer to μg free base/litre of plasma, are uncorrected for losses in recovery up to 30 per cent. In two studies arterial oxygen saturation was determined spectrophotometrically (Nahas, 1951).

RESULTS

Table I shows some typical features of apnoeic oxygenation. The severe respiratory acidosis which develops progressively over a period of 60 minutes, as demonstrated by a pronounced fall in arterial pH and rise in P_{CO_2}, is accompanied by a rise in circulating catecholamine concentration. In the early period an increase in plasma noradrenaline is more pronounced, after which the adrenaline level rises markedly. Except for a high initial "standard" bicarbonate, and a less pronounced rise in catecholamine levels, the findings shown in table I are essentially as described previously (Millar, 1960).

Table II, by contrast, presents the data from an experiment in which a solution of T.H.A.M. (0.33M.) was given by intravenous infusion during apnoeic oxygenation, and shows that a much smaller fall in pH occurred, from an initial value of 7.45 to only 7.24 after 60 minutes of apnoea; during this time arterial P_{CO_2} increased from 30 to 130 mm Hg, and the buffering action of T.H.A.M. was evident in a pronounced rise in "standard" bicarbonate from 21 to 49 m.mole/l. During this period plasma catecholamine concentration showed only small changes, but when the infusion of buffer amine was discontinued greatly increased levels of adrenaline and noradrenaline accompanied the reduced pH and elevated P_{CO_2} which occurred after a further 30 minutes of apnoea.

Table III illustrates the findings from a similar study in which the rise in P_{CO_2} produced by apnoeic oxygenation was buffered more effectively by a 0.66M. solution of T.H.A.M.; after 117 minutes of apnoea the arterial pH was 7.50, and

TABLE I

Changes in arterial pH, P_{CO_2}, "standard" bicarbonate, adrenaline (A) and noradrenaline (N) concentrations, and arterial blood pressure (B.P.) during 60 min of apnoeic oxygenation (A.O.) in one experiment.

Time (min)	Sample	pH	P_{CO_2} (mm Hg)	"Standard" bicarbonate (m-mole/l.)	A (μg/l.)	N (μg/l.)	B.P. (mm Hg)	
							Systolic	Diastolic
	1	7.46	45	29	0.02	0.33	166	126
Start A.O.								
+15	2	7.05	140	33	0.22	0.97	211	109
+30	3	6.88	245	38	3.7	2.6	223	136
+60	4	6.67	395	36	8.0	2.2	140	75

TABLE II

Arterial pH, P_{CO_2}, "standard" bicarbonate, adrenaline (A) and noradrenaline (N) concentrations, and mean arterial blood pressure (M.A.B.P.) before, during and after 60 min of apnoeic oxygenation (A.O.) buffered by a 0.33M. solution of T.H.A.M.

Time (min)	Sample	pH	P_{CO_2} (mm Hg)	"Standard" bicarbonate (m-mole/l.)	A (μg/l.)	N (μg/l.)	M.A.B.P. (mm Hg)
	1	7.45	30	21	0.12	0.73	146
Start A.O. + T.H.A.M.							
+15	2	7.44	63	40	0.05	0.43	152
+30	3	7.32	97	42	0.30	0.64	140
+60	4	7.24	130	49	0.34	0.59	131
+105	5	7.25	(145)	(<50)	0.48	0.36	127
Stop T.H.A.M.							
+30	6	6.92	285	50	14.5	5.5	188

TABLE III

Arterial pH, P_{CO_2}, "standard" bicarbonate, adrenaline (A) and noradrenaline (N) concentrations, and mean arterial blood pressure (M.A.B.P.) during 117 min of apnoeic oxygenation (A.O.) buffered by T.H.A.M. (0.66M.)

Time (min)	Sample	pH	P_{CO_2} (mm Hg)	"Standard" bicarbonate (m-mole/l.)	A (μg/l.)	N (μg/l.)	M.A.B.P. (mm Hg)
	1	7.54	26	22	0	0.45	152
Start T.H.A.M.							
+15	2	7.94	10	34	0	0.40	110
Start A.O.							
+15	3	7.87	25	40	0.07	0.25	112
+30	4	7.79	30	44	0.11	0.10	122
+60	5	7.69	43	48	0.12	0.29	127
+117	6	7.50	(75)	(>50)	0.71	0.95	143
Remove O_2							
+8	7	7.46	(87)	(>50)	10.5	7.8	147
+13	8	7.36	98	50	74.1	24.8	Zero

TABLE IV

The use of T.H.A.M. (0.66M.) in maintaining P_{CO_2} almost constant at an increased arterial pH during 1 hour of apnoeic oxygenation (A.O.)

Time (min)	Sample	pH	P_{CO_2} (mm Hg)	"Standard" bicarbonate (m-mole/l.)	M.A.B.P. (mm Hg)
	1	7.47	43	29	118
Start A.O. + T.H.A.M.					
+15	2	7.78	28	40	109
+30	3	7.84	28	46	134
+60	4	7.74	39	50	221

P_{CO_2} approximately 75 mm Hg. For the first hour plasma adrenaline and noradrenaline showed negligible changes, and only moderate increases were measured after nearly 2 hours of respiratory arrest.

The ability of T.H.A.M. to maintain P_{CO_2} almost constant but at an increased arterial pH, in the course of 1 hour of apnoeic oxygenation, is well shown by the study illustrated in table IV.

In two experiments the initial period of ventilation with 100 per cent oxygen (prior to apnoea) was continued for a further 15 minutes while T.H.A.M. was given; in one instance (table III) this produced a fall in P_{CO_2} from 26 to 10 mm Hg, accompanied by a marked rise in pH and "standard" bicarbonate, without change in catecholamine levels. In the other experiment (table VII) the changes in pH and "standard" bicarbonate were even more pronounced, and obviously represent the effects of an overdose of T.H.A.M. when given in the absence of respiratory acidosis.

An abrupt and pronounced fall in plasma catecholamine levels occurred as a result of T.H.A.M. administration as shown in table V, which presents the results from three experiments in which the infusion of buffer amine (0.66M.) was begun after apnoeic oxygenation had already lasted for periods of 45, 50, and 60 minutes respectively. The rapidity of the changes induced by T.H.A.M. are well illustrated by one of these studies in which a fall in P_{CO_2} from 315 to 52 mm Hg occurred over 10 minutes, accompanied by a 100 per cent rise in "standard" bicarbonate, an increase of 1 unit in whole blood pH, and a fall in total plasma catecholamine concentration from 7 to 1.4 μg/l.

The alterations in systolic and diastolic blood pressure induced in a typical experiment by unbuffered apnoeic oxygenation are included in table I and, as observed previously (Millar, 1960), there was an initial decrease in diastolic level accompanied and followed by marked increases in systolic pressure, but after 1 hour of apnoea blood pressure was reduced. When apnoeic oxygenation was buffered concurrently by T.H.A.M., the average systolic and diastolic pressure in five experiments increased progressively to reach levels, after 1 hour of apnoea, which were 16 per cent and 24 per cent above control values respectively. Blood pressure changes were quite inconsistent, however; for example, pronounced hypertension occurred in two experiments with peaks at 30 and 60 minutes respectively, although P_{CO_2} levels at these times were only 30 and 39 mm Hg (tables VII and IV); table II shows, by contrast, that although in another experiment there was a steady increase in P_{CO_2} to 145 mm Hg during 105 minutes of buffered apnoeic oxygenation, the concomitant changes in mean arterial blood pressure were relatively small. A variable response was also shown when the infusion of buffer amine was started after apnoea had already been maintained for some time (table V); the mean blood pressure levels increased, fell, or remained unchanged.

In two experiments (tables III and VII) a fall in mean arterial blood pressure resulted when T.H.A.M. (0.66M.) was infused rapidly during 15 minutes of manual ventilation with 100 per cent oxygen (prior to apnoeic oxygenation).

Tables VI and VII give the complete data obtained in two experiments in which arterial oxygen saturation was measured in addition to pH, P_{CO_2} and "standard" bicarbonate. Table VI shows the gradual decline in oxygen saturation which characteristically accompanies the progressive alveolar carbon dioxide accumulation induced by apnoeic oxygenation, and illustrates the return

TABLE V

Changes in arterial pH, P_{CO_2}, "standard" bicarbonate, adrenaline (A) and noradrenaline (N) concentrations, and mean arterial blood pressure (M.A.B.P.) when an infusion of T.H.A.M. (0.66M.) was given during an existing severe respiratory acidosis (A.O.-apnoeic oxygenation).

Time (min)	pH	P_{CO_2} (mm Hg)	"Standard" bicarbonate (m-mole/l.)	A (μg/l.)	N (μg/l.)	M.A.B.P. (mm Hg)
A.O. +45	6.72	325	34	24.9	10.2	215
T.H.A.M. +5	7.09	145	38	1.0	1.4	121
A.O. +50	6.62	315	24	5.4	1.6	49
T.H.A.M. +10	7.62	52	49	0.22	1.2	91
+45	7.74	(47)	(>50)	0.03	0.43	118
A.O. +60	6.67	395	36	8.0	2.2	97
T.H.A.M. +20	7.17	(180)	(>50)	0.53	1.2	97

TABLE VI

Arterial oxygen saturation, arterial pH, P_{CO_2} and "standard" bicarbonate, and mean arterial blood pressure (M.A.B.P.) during and after apnoeic oxygenation (A.O.) buffered by T.H.A.M. (0.66M.)

Time (min)	Sample	pH	P_{CO_2} (mm Hg)	"Standard" bicarbonate (m-mole/l.)	O_2 sat. %	M.A.B.P. (mm Hg)
	1	7.44	36	23	100	162
Start A.O.						
+15	2	6.97	150	29	96	163
+30	3	6.87	250	30	95	206
+60	4	6.59	366	27	81	95
Start T.H.A.M.						
+15	5	7.10	164	44	102	123
+30	6	7.40	(110)	(>50)	99	116
+60	7	7.43	(105)	(>50)	101	105
Remove O_2						
+6	8	7.20	(170)	(>50)	33	

TABLE VII

Arterial oxygen saturation, arterial pH, P_{CO_2} and "standard" bicarbonate, and mean arterial blood pressure (M.A.B.P.) during and after apnoeic oxygenation (A.O.) buffered by T.H.A.M. (0.66M.)

Time (min)	Sample	pH	P_{CO_2} (mm Hg)	"Standard" bicarbonate (m-mole/l.)	O_2 sat. %	M.A.B.P. (mm Hg)
	1	7.52	23	19	95	147
Start T.H.A.M.						
+15	2	8.00	13	34	99	114
Start A.O.						
+15	3	7.94	20	43	96	170
+30	4	7.84	30	49	94	210
+60	5	7.71	(50)	(>50)	94	168
Stop T.H.A.M.						
+14	6	7.34	(120)	(>50)	90	97
+44	7	7.04	205	48	57	74
Vent.						
+6	8	7.64	35	36	97	Zero

to full oxygenation which follows T.H.A.M. administration. Table VII demonstrates that the buffer amine is also effective in maintaining oxygenation for at least 1 hour of apnoea, and shows the decline in arterial oxygen saturation which results when the infusion of T.H.A.M. is stopped. Similar changes were readily apparent in other experiments from inspection of arterial blood samples withdrawn before or after infusion of T.H.A.M. during apnoeic oxygenation.

There was no evidence, on the other hand, that the buffer amine could permit survival for an extended period when apnoea was maintained with the airway open to room air rather than to the 100 per cent oxygen available during true apnoeic oxygenation, and in six experiments the average period of "apnoea in air" lasted for only 7.5 minutes (range 4–13 minutes), during which plasma catecholamine levels were greatly increased, before cardiac arrest occurred from acute asphyxia (tables III and VI).

In eight of the nine experiments there was no indication, from the intra-arterial blood pressure record, that cardiac arrhythmias occurred either in direct association with administration of T.H.A.M., or because of the sudden changes in P_{CO_2} and pH which resulted. During the final experiment, however (table VII), 75 mg thio-

pentone was injected during a period of hypertension, after 39 minutes of apnoeic oxygenation buffered by T.H.A.M.; this caused abrupt hypotension (associated with rapid ventricular arrhythmias). Gentle pressure on the thoracic cage during palpation of the cardiac impulse resulted in an immediate return of blood pressure to the previous hypertensive level. Later in this experiment there was a fall in arterial oxygen saturation to 57 per cent after terminating the infusion of T.H.A.M., and complete circulatory collapse occurred during the subsequent period of ventilation with 100 per cent oxygen (immediately prior to withdrawal of sample 8, table VII).

After an initial "lag" period of about 15 minutes an infusion of T.H.A.M. induced a profound diuresis; in the single experiment during which urine was drained by catheter the amount excreted was 1,170 ml compared to a total of 1,075 ml administered intravenously.

DISCUSSION

These experiments confirm the effectiveness of an organic buffer amine, T.H.A.M., in limiting or preventing the extreme respiratory acidosis induced by apnoeic oxygenation, when given by infusion throughout the period of apnoea. Instead of a greatly increased P_{CO_2}, bicarbonate is formed in large amounts according to the equation.

$$R-NH+CO_2+H_2O \rightleftharpoons HCO'_3+\overset{+}{R}NH_2$$

(Krebs, 1951). In this study, the average HCO'_3/H_2CO_3 ratio in the course of 45–90 minutes of unbuffered apnoeic oxygenation was 2.9; when T.H.A.M. was infused throughout comparable periods of apnoea the ratio was increased to 17.3. As a result of this marked rise in HCO'_3/H_2CO_3 ratio, the fall in arterial pH was minimized or prevented. If sufficient buffer amine was given pH was increased. For example, when the 0.33M. solution was used, arterial pH was approximately 7.2 at a P_{CO_2} of 100-150 mm Hg, after 60 minutes of apnoea, whereas with the 0.66M. solution P_{CO_2} could be held below 50 mm Hg for at least 1 hour of apnoea, but only at the price of an increased pH. When arterial pH and P_{CO_2} were not elevated, infusion of T.H.A.M. induced a condition of "metabolic alkalosis."

An additional feature of the action of T.H.A.M. is that while untreated apnoeic oxygenation is always accompanied by anuria (Kopecky et al., 1952), concurrent (or subsequent) T.H.A.M. administration induces a marked diuresis which, according to Nahas and Rosen (1959), eliminates in the form of bicarbonate up to 28 per cent of the estimated total carbon dioxide produced during apnoea.

When the respiratory acidosis was buffered, plasma adrenaline and noradrenaline were held at near-normal levels, arterial oxygen saturation was maintained, and changes in arterial blood pressure were minimized. Unfortunately there is insufficient evidence from this, or from our previous study, to show clearly whether the fall in pH or the rise in carbon dioxide tension was mainly responsible for the changes in plasma catecholamine levels during apnoeic oxygenation. However, when pH was reduced during unbuffered apnoeic oxygenation, P_{CO_2} levels of 100–200 mm Hg were always accompanied by definite increases in plasma adrenaline and noradrenaline, whereas when P_{CO_2} values were in the same range after prolonged apnoea buffered by T.H.A.M. (the fall in pH being less), catecholamine levels were frequently not greatly changed. This merely suggests that a reduction in pH may be the more important factor in liberating increased amounts of adrenaline and noradrenaline.

The plasma catecholamine concentrations measured during buffered and unbuffered apnoeic oxygenation, as described in this and the previous paper (Millar, 1960), appear to be in line with the report by Jordan et al. (1959), who measured similar levels using the controversial ethylenediamine technique of assay.

When apnoeic oxygenation has continued for an hour or longer a very rapid fall in arterial P_{CO_2} can be produced by manual overventilation; at the same time the increased catecholamine levels are lowered to near-normal values (Millar, 1960). Rapid infusion of T.H.A.M., after a period of apnoeic oxygenation, is comparable to overventilation in its effect on arterial pH, P_{CO_2}, and circulating catecholamines, although the marked rise in "standard" bicarbonate produced by T.H.A.M. contrasts with the fall to low levels (indicative of a metabolic acidosis) when respiratory acidosis is corrected by overventilation.

The absence of cardiac arrhythmias during

reduction in plasma P_{CO_2} by infusion of T.H.A.M. reinforces the findings of previous experiments in which there were no serious cardiac effects during rapid reduction in arterial P_{CO_2} by ventilation with 100 per cent oxygen (Holmdahl, 1956; Millar, 1960). It deserves re-emphasis, therefore, that the initial evidence implicating rapid reduction in arterial P_{CO_2} as a cause of serious ventricular arrhythmias was obtained when dogs breathed 30–40 per cent carbon dioxide in oxygen for 3–4 hours and were then suddenly made to breathe room air (Brown and Miller, 1952), a transition which could result in an abrupt (although probably transient) reduction in arterial oxygen saturation.

The occurrence of acute circulatory collapse in one experiment of the present study seems to underline the importance of an anoxic factor, since the degree of arterial oxygen desaturation reached earlier had been more extreme than in any of the other fifteen experiments from this and the previous study (all of which were uncomplicated by circulatory failure). Ventricular arrhythmias can be induced readily in dogs by a variety of stimuli, and not infrequently their appearance and disappearance can be related to inflation of the lungs. The fast ventricular rhythm (accompanied by hypotension), which occurred after injection of thiopentone during apnoeic oxygenation (also in the last mentioned experiment), was apparently reversed by external pressure on the cardiac apex; this emphasizes the sensitivity of the dog heart to a stimulus which in this case was predominantly mechanical in nature. It appears, therefore, that the available data should be re-examined and further evidence obtained before a fall in P_{CO_2} per se (i.e. uncomplicated by mechanical factors or by preceding or concurrent arterial oxygen desaturation) can be accepted as a primary cause of cardiovascular collapse.

The action of T.H.A.M. in maintaining full oxygen saturation during apnoea, or in restoring oxygenation during an already existing respiratory acidosis, appears to be secondary to the reduction in alveolar P_{CO_2} which in turn results from the buffering of accumulated carbon dioxide in blood, body fluids and tissues. Since in this study the preliminary period of denitrogenation by spontaneous or controlled ventilation with 100 per cent oxygen was short, the effect of T.H.A.M. on oxygen saturation during apnoea shows that accumulation of nitrogen in the alveoli is of minor importance in affecting oxygenation compared to the progressive accumulation of carbon dioxide. Provided that sufficient T.H.A.M. is given it seems likely that apnoeic oxygenation could be prolonged for considerably longer than the maximum period of just under 2 hours studied in these experiments.

When the recommended 0.33M. solution of T.H.A.M. is given to buffer a severe respiratory acidosis, a fast rate of infusion will be required and this may be difficult to maintain. Venous irritation and occasional haemolysis detract from the greater convenience of the 0.66M. solution, which in addition may produce a marked alkalosis unless the amount infused is carefully titrated.

SUMMARY

When given by intravenous infusion throughout periods of apnoea lasting for 1 hour or longer, solution of tris-(hydroxymethyl) amino-methane (T.H.A.M.) were effective in limiting or preventing the extreme fall in pH induced by accumulation of carbon dioxide. Rises in plasma adrenaline and noradrenaline were prevented, arterial oxygen saturation was maintained, and the changes in arterial blood pressure induced by apnoeic oxygenation were not observed.

When administered during an existing severe respiratory acidosis, solutions of T.H.A.M. produced a rapid fall in P_{CO_2}, a rise in arterial pH, a marked increase in "standard" bicarbonate (and in the HCO'_3/H_2CO_3 ratio), a rise in arterial oxygen saturation, and an abrupt fall in plasma adrenaline and noradrenaline concentrations. These changes were discussed briefly.

ACKNOWLEDGMENTS

The technical assistance of Mrs. J. C. Joba is gratefully acknowledged. Tris-(hydroxymethyl) amino-methane was supplied by Abbott Laboratories, Montreal. These studies were partly supported by a grant from Parke Davis and Company.

REFERENCES

Astrup, P. (1956). A simple electrometric technique for the determination of carbon dioxide in blood and plasma, total content of carbon dioxide in plasma and bicarbonate content in "separated" plasma at a fixed carbon dioxide tension (40 mm Hg). *Scand. J. clin. Lab. Invest.*, **8**, 33.

Astrup, P., and Schroder, S. (1956). Apparatus for anaerobic determination of the pH of blood at 38 degrees centigrade. *Scand. J. clin. Lab. Invest.*, **8**, 30.

Brown, E. B., and Miller, F. (1952). Ventricular fibrillation following a rapid fall in alveolar carbon dioxide concentration. *Amer. J. Physiol.*, **169**, 56.

Draper, W. B., Whitehead, R. W., and Spencer, J. N. (1947). Studies on diffusion respiration. III: Alveolar gases and venous blood pH of dogs during diffusion respiration. *Anesthesiology*, **8**, 524.

Holmdahl, M. H. (1956). Pulmonary uptake of oxygen, acid-base metabolism, and circulation during prolonged apnoea. *Acta chir. scand.*, Suppl., **212**, 1.

Jordan, E. C., Mehlman, B., Nahas, G. G. (1959). The buffering of CO_2 by T.H.A.M., during hypercapnia. Effects on the circulation. *Fed. Proc.* **18**, 78.

Kopecky, F. A., Rayburn, C. J., Whitehead, R. W., and Draper, W. B. (1952). Study of anuria occurring during apnoea under diffusion respiration. *Amer. J. Physiol.*, **168**, 131.

Krebs, H. A. (1951). The use of "CO_2 Buffer" in manometric measurement of cell metabolism. *Biochem. J.*, **48**, 349.

Millar, R. A. (1960). Plasma adrenaline and noradrenaline during diffusion respiration. *J. Physiol.*, **150**, 79.

—— Keener, E. B., and Benfey, B. G. (1959). Plasma adrenaline and noradrenaline after phenoxybenzamine administration, and during haemorrhagic hypotension, in normal and adrenalectomized dogs. *Brit. J. Pharmacol.*, **14**, 9.

Nahas, G. G. (1951). Spectrophotometric determination of hemoglobin and oxyhemoglobin in whole hemolyzed blood. *Science*, **113**, 723.

—— Rosen, H. (1959). The buffering of CO_2 by T.H.A.M. during hypercapnia. Effects on acid-base balance. *Fed. Proc.*, **18**, 111.

BOOK REVIEW

Essays on the first Hundred Years of Anaesthesia. By W. Stanley Sykes. Published by E. and S. Livingstone Ltd., Teviot Place, Edinburgh. Price 30*s*.

Dr. Sykes has written a most interesting book alike for the layman and the professional. How original many of his ideas are I am unable to say, but some at least seem so to me; here for instance are two: (1) A long preface giving an account of many inventions. This should be studied by every would-be inventor, it is more than likely it would save him a lot of trouble. (2) A chapter on the environment of anaesthesia. I think this must be an original idea, but one nevertheless very much to the point. It sets the stage.

Chapter three deals with the "Beginnings of things" about which so much has already been written that Dr. Sykes was a brave man to make another attempt. He has succeeded in giving us an interesting account into which he has obviously put some of the Herculean labours to which he refers in his dedication to "Nan".

He shows us Queen Victoria in a light as unusual as it is delightful, and he goes back to Sir Walter Raleigh for the earliest acquaintance of the western European world with curare. A more appropriate quotation for the chapter headed "Stupidities" could hardly be found; here it is: "Against stupidity the gods themselves battle in vain". Not the whole truth let us hope but, regrettable as it is, a large element of it. Most of the examples of stupidity given are attributed to surgeons, which is explained by the fact that they would keep talking about a subject of which they knew little. The greatest stupidity of all that surgeons as a body (there were a few, a very few, enlightened exceptions) made and to which Dr. Sykes does not call attention, except indirectly, derived from their too great attention to their self-regarding instincts. All they cared about was to have a sufficient number of skilled technicians so that they should never be inconvenienced by delay. The idea that they had a part to play, or a duty to perform in the advancement of anaesthesia, and surgery dependent on that advance, apparently never occurred to them. The consequence was that the tremendous development that has taken place in the last few years in anaesthesia and surgery had to await the arrival of a more enlightened, because less selfish, generation. The history of the various factors which wrought this change would form a very interesting chapter, so perhaps we may expect it in volume two. Before I finish with this account of stupidities I must quote the example taken from the famous

[*continued on page* 261

Brit. J. Anaesth. (1960), **32**, 256

OBSERVATIONS ON A REBREATHING TECHNIQUE FOR THE DETERMINATION OF ARTERIAL P_{CO_2} IN THE APNOEIC PATIENT

BY

M. K. SYKES

Department of Anaesthesia, Postgraduate Medical School and Hammersmith Hospital, London, W.12

EQUILIBRIUM between mixed venous blood and lung gas can be achieved by rebreathing a suitable carbon dioxide mixture from a bag. Plesch (1909) was the first to use this principle for the determination of mixed venous carbon dioxide tension ($P\bar{v}_{CO_2}$). For some years the method was employed in the determination of cardiac output but it was later realized that the accuracy was insufficient for this purpose (Grollman, 1932; Collier, 1956; Defares, 1956, 1958). Further interest in the method was stimulated by the theoretical analysis of Suskind and Rahn (1954). They pointed out that the mixed venous carbon dioxide tension is predominantly controlled by the alveolar ventilation and is little affected by changes in cardiac output. A corollary is that the arteriovenous P_{CO_2} difference is small and relatively constant.

The use of rapid gas analyzers has facilitated more detailed studies of the rebreathing process. In 1956 Collier showed that a "plateau" may be observed in the P_{CO_2} trace when equilibrium is complete (fig. 1, C). To achieve this state before appreciable recirculation occurs the bag must be kept small and the initial P_{CO_2} of the rebreathed gas must be within 15 mm Hg of the $P\bar{v}_{CO_2}$. Hackney, Sears and Collier (1958) continued this work and showed that a close estimate of arterial P_{CO_2} could be obtained by subtracting a figure of 6 mm Hg from the $P\bar{v}_{CO_2}$ obtained by the rebreathing method. Comparison of such estimates with direct arterial blood gas analyses in sixty patients with heart and lung disease revealed that the standard error was ± 2.9 mm Hg with a maximum observed discrepancy of ± 5.3 mm Hg. The value obtained by the rebreathing method yielded a more accurate estimate than end-tidal P_{CO_2} when disturbances of the ventilation-perfusion ratio were present.

Although the Collier technique can be applied with success to clinical practice (Griggs et al., 1958) a rapid gas analyzer is essential. This is both cumbersome and expensive. Campbell and Howell (1960a) have now modified the technique so that the gas may be analyzed on a simplified

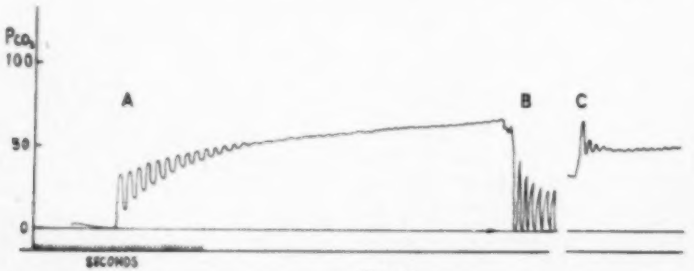


FIG. 1

Continuous P_{CO_2} trace recorded by mass spectrometer during rebreathing. Subject connected by a three-way tap to a 2-l. bag containing 100 per cent oxygen. The third limb of the tap was open to air. Sample (15 ml/min) was taken from the mouthpiece. Spontaneous respiration.
A—initial period of rebreathing.
B—tap open to air.
C—period of equilibration showing "plateau".
Ordinate—P_{CO_2}. Abscissa—time in seconds.

Haldane apparatus (Campbell, 1960); the percentage of carbon dioxide can be read directly from the burette and converted to P_{CO_2} from the formula:

$$P_{CO_2} = \frac{(B-47) \times \%CO_2}{100}$$

where B = the barometric pressure in mm Hg.

The modified technique is carried out in three stages. First, a gas mixture suitable for the subsequent equilibration is prepared by rebreathing into a bag containing oxygen (fig. 1, A). A pause is then made to allow the patient to eliminate excess carbon dioxide retained in the body during this period (fig. 1, B). In the third stage, which must obviously be accomplished before appreciable recirculation of blood occurs, the prepared gas mixture is equilibrated with the mixed venous blood (fig. 1, C). $\bar{P}v_{CO_2}$ is calculated from the analysis of the gas remaining in the bag. By subtracting 6 mm Hg from this figure an estimate of Pa_{CO_2} is obtained.

Consideration of the mechanisms involved (Campbell and Howell, 1960b) suggests that inadequate gas exchange between bag and lungs is the most likely cause of failure. Since the tidal volume is under the control of the operator when artificial ventilation is employed (except where gross obstructive lesions exist) it would seem that the technique could be most usefully adapted to the apnoeic patient. Studies have been made to determine the effectiveness of the technique under such circumstances; they form the subject of this communication.

METHODS

The experiments were performed on patients suffering from severe tetanus who were being treated by total paralysis and intermittent positive pressure respiration. Patients were studied at various stages during therapy. Chest complications such as bronchitis, bronchopneumonia or atelectasis were present in many of the cases studied.

The airway was secured in all cases by tracheostomy. A cuffed rubber tube was used in the adults and children studied, whilst a short latex armoured tube was used in the neonates. If an audible leak around the tube occurred the experiment was discarded. All patients were maintained in a steady respiratory state for at least 15 minutes before observations were commenced. Tracheal suction, changes of position and of inflating pressure were avoided during the experiment.

As a rapid gas analyzer was not available, individual 10-ml samples were analyzed, either on the standard or modified Haldane apparatus. Twenty analyses of the same gas on the latter apparatus were never in error by more than 0.1 per cent carbon dioxide when compared with the value obtained by analysis on the standard Haldane (4.88 per cent carbon dioxide in oxygen). Since an error of ± 3 mm Hg P_{CO_2} was considered acceptable this degree of accuracy proved adequate for clinical purposes.

Preliminary experiments were performed to determine the optimal conditions for the preparation of the equilibrating gas mixture. The conclusions are set out in table I. Standard anaesthetic bags of 2 l. and 500 ml were used for adults and children whilst a 100-ml child's balloon of good quality proved satisfactory for the neonates. The recommendations were tested by examining each of the three phases separately.

(1) *Preparation of the equilibrating gas sample.*

In adults the rise in carbon dioxide concentration in the bag was determined by analyzing 15-ml samples aspirated into evacuated sampling tubes during an expiratory pause. In children and neonates the removal of such relatively large samples would have affected the results. Rebreathing was therefore stopped after 15 seconds

TABLE I

	Rebreathing				Equilibrations	
Subjects	Bag size	Tidal volume	Frequency	Duration	Duration 1st	Duration 2nd
Adults	2 l.	500 ml	20/min	90 sec	21 sec	42 sec
Children 6–12 yrs.	500 ml	250 ml	30/min	75 sec	16 sec	32 sec
Neonates	100 ml	40 ml	60/min	60 sec	10 sec	20 sec

and the bag gas analyzed. The bag was flushed and refilled with oxygen and another analysis made after 30 seconds rebreathing. The patient was reconnected to the respirator for a period of 5 minutes while each analysis was proceeding. Further samples were obtained in this manner until the desired curve had been completed.

Results. Thirty-two curves were obtained from six adults, three children and twelve neonates. The neonates were between five days and one month old. The rise of carbon dioxide concentration in samples taken from the bag is plotted in figures 2 and 3. The initial rise in carbon dioxide concentration is rapid; the curve then flattens out when equilibrium with mixed venous blood is achieved. But recirculation is now occurring. The slope of the more horizontal portion of the curve is therefore representative of the rate of carbon dioxide production by the body. The mean rise (calculated over the period 90–120 seconds from twelve neonate curves and 75–135 seconds in the six adult curves) was 9.7 mm Hg/min in neonates (S.D. 2.22 mm Hg) and 8.3 mm Hg/min in adults (S.D. 2.35 mm Hg).

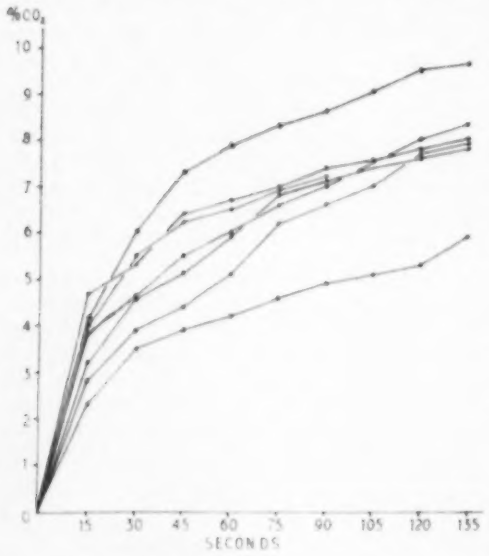


FIG. 2
Rise in carbon dioxide percentage in a bag filled with 2 l. of 100 per cent oxygen during initial rebreathing period. Apnoeic adults. Tidal volume approximately 500 ml. Respiration rate 20/min.
Ordinate—per cent carbon dioxide.
Abscissa—time in seconds.

(2) *The rate of return to the pre-existing* $\bar{P}v_{CO_2}$ *level after preparation of the equilibrating gas.*

Previous unpublished observations on apnoeic adult patients suggested that the Pv_{CO_2} would return to the level existing before rebreathing within 2 minutes. To confirm this in the neonate (when no fast analyzer was available) it was necessary to use a rather cumbersome technique

The $\bar{P}v_{CO_2}$ was first determined as described in section 3, using a second equilibration to check the completeness of the first. Several 100-ml balloons were then filled from a large bag containing a carbon dioxide and oxygen mixture having a Pco_2 within 10 mm Hg of this value. A 60-seconds period of rebreathing using a fresh balloon filled with oxygen was then performed. At minute intervals after the patient had been reconnected to the respirator one of the prepared balloons was connected to the patient for a period of 10 seconds and an equilibration performed. subsequent analysis of the balloons in three experiments (fig. 4) suggested that the original level of $\bar{P}v_{CO_2}$ had been reached within 3 minutes of discontinuing the period of rebreathing.

(3) *The time required to reach final equilibrium.*

The duration of equilibration is governed by the occurrence of recirculation of the major portion of the blood. In the resting adult the lung-to-lung circulation time is approximately 21 seconds (Best and Taylor, 1955). In the neonate and infant (Hubbard, Preston and Ross, 1942) it appears that this time may vary from 3 to 12 seconds depending on the age. Intermediate values of 5 to 17 seconds are suggested by Hubbard for children from 2 to 12 years.

The attainment of equilibrium was tested in two ways:

(1) The percentage carbon dioxide in the bag at the end of the first equilibration was compared with that obtaining after the bag had been reapplied for a similar period of time.

(2) A similar set of experiments was performed using a second period of equilibration which was twice as long as the first. The rise in Pco_2 resulting from this extended period of equilibration should be no more than 4 mm Hg. A rise

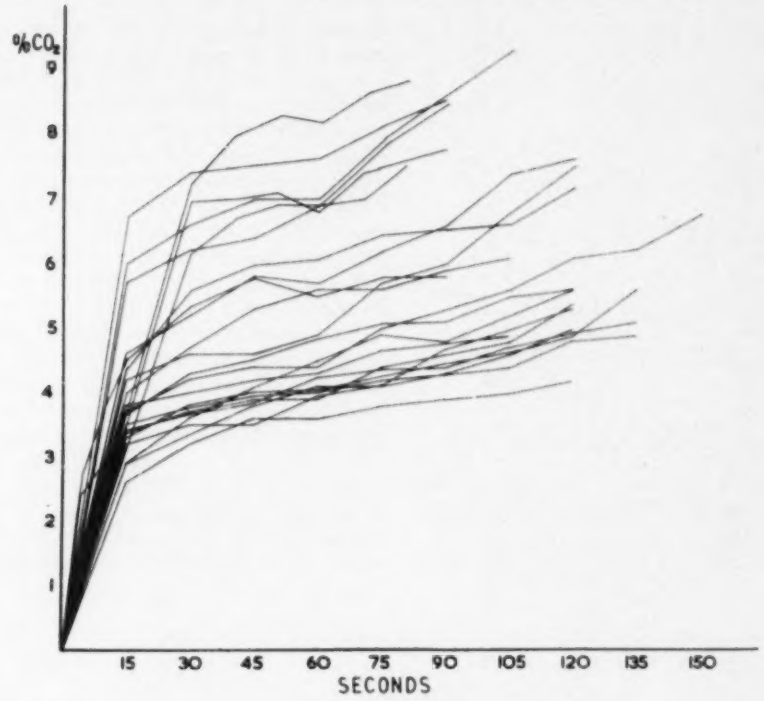


FIG. 3

Rise in carbon dioxide percentage in a bag filled with 100 ml of 100 per cent oxygen during initial rebreathing period. Apnoeic neonates. Tidal volume approximately 40 ml. Respiration rate 60 per minute.
Ordinate—per cent carbon dioxide. Abscissa—time in seconds.

greater than this would indicate incomplete equilibration during the first period. In both sets of experiments a fall in P_{CO_2} would suggest that the initial P_{CO_2} of the equilibrating gas mixture was too high.

Results. (1) These are shown in figure 5, C-B. The mean of the differences in adults was 0.10 per cent carbon dioxide, S.D. 0.25 per cent carbon dioxide, whilst in neonates the corresponding figures were 0.009 per cent carbon dioxide, S.D. 0.14 per cent carbon dioxide.

(2) Figure 5 C'-B. The mean of the differences was 0.02 per cent carbon dioxide, S.D. 0.02 per cent carbon dioxide in neonates and 0.07 per cent carbon dioxide, S.D. 0.03 per cent carbon dioxide in adults. It is apparent that equilibrium had been reached by the end of the first period in the majority of instances.

CONCLUSIONS

From these results, it is concluded that this method can be successfully applied to the apnoeic patient. It can also be used in the anaesthetized patient if suitable methods are employed for the estimation of carbon dioxide in the presence of anaesthetic agents (Nunn, 1958). The advantages of cheapness, simplicity and speed will, however, be nullified if the method is not used with intelligence. In the present state of our knowledge, it would seem that failure to reach equilibrium is the most likely cause of inaccuracy. It is also conceivable that a false plateau may occur if the initial P_{CO_2} of the rebreathed gas is too high. Both of these occurrences can be detected by repeating the equilibration for double the previous period. Recirculation will cause a small rise in the P_{CO_2} in the bag during the

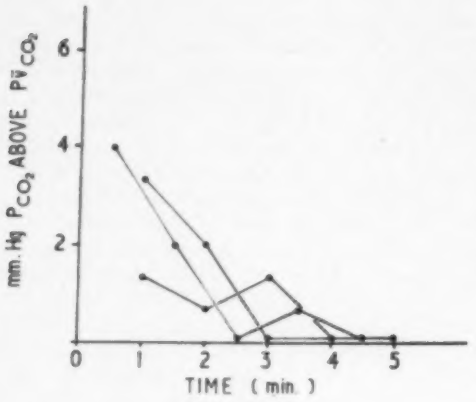


FIG. 4

To show the rate at which the $\bar{P}v_{CO_2}$ returns to normal when the patient is reconnected to the respirator after a period of 60 seconds rebreathing. Observations on three neonates.
Ordinate—mm Hg P_{CO_2} above original $\bar{P}v_{CO_2}$.
Abscissa—time (minutes).

extended period of equilibration but this is unlikely to be more than 3–4 mm Hg.

If the P_{CO_2} at the conclusion of the second equilibration period is more than 5 mm Hg above that obtained during the first equilibration the whole experiment should be repeated using a longer initial period of rebreathing or a smaller initial bag volume. The reverse applies if the second P_{CO_2} is smaller than the first. Even when such repetition is necessary the final value will still be obtained more quickly than the result of an arterial blood gas analysis.

Final assessment of the method can only be made by comparing the results with direct determinations of arterial P_{CO_2} in a large number of cases with lung abnormalities. Such a study is in progress and will be reported at a later date.

SUMMARY

A modified rebreathing technique is described for the determination of the Pa_{CO_2} in the apnoeic patient. Providing suitable adjustments are made,

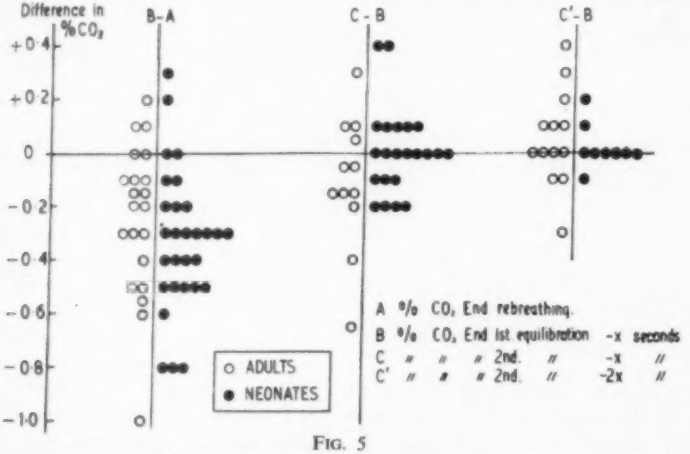


FIG. 5

The attainment of final equilibrium. Analysis of bag gas for percentage carbon dioxide.
A—at the end of the period of rebreathing.
B—at the end of the first period of equilibration (neonates 10 seconds, adults 21 seconds).
C—at the end of the second period of equilibration (neonates 10 seconds, adults 21 seconds).
C'—at the end of the second period of equilibration (neonates 20 seconds, adults 42 seconds).
The first column (B-A) shows the fall in per cent carbon dioxide during the first equilibration. The second column (C-B) represents the difference between two equilibrations of equal duration. The third column (C'-B) represents the difference between two equilibrations, the second being twice as long as the first.

the method appears to give satisfactory results in neonates, children and adults.

ACKNOWLEDGMENT

The work was performed in the Tetanus Unit (Director, Professor E. B. Adams) at King Edward VIII Hospital, Durban, South Africa. The project is being financed by the Wellcome Trust. Thanks are due to Mr. H. C. Whittle for help with the gas analyses and to the Association of Anaesthetists for the provision of a Haldane apparatus.

REFERENCES

Best, C. H., and Taylor, N. B. (1955). *The Physiological Basis of Medical Practice*. 6th ed., p. 177. London: Baillière, Tindall & Cox.

Campbell, E. J. M. (1960). Simplification of Haldane's apparatus for measuring CO_2 concentration in respired gases in clinical practice. *Brit. med. J.* **1**, 457.

Campbell, E. J. M., and Howell, J. B. L. (1960a). Simple rapid methods of estimating arterial and mixed venous P_{CO_2}. *Brit. med. J.*, **1**, 458.

—— —— (1959b). *A Symposium on pH and Blood Gas Measurement: Methods and Interpretation*, edited by R. F. Woolmer. London: Churchill.

Collier, C. R. (1956). Determination of mixed venous CO_2 tension by rebreathing. *J. appl. Physiol.*, **9**, 25.

Defares, J. G. (1956). *A Study of the Carbon Dioxide Time Course during Rebreathing* (Thesis). Utrecht, Netherlands.

—— (1958). Determination of $\bar{P}v_{CO_2}$ from the exponential CO_2 rise during rebreathing. *J. appl. Physiol.*, **13**, 159.

Griggs, D. E., Hackney, J. D., Collier, C. R., and Affeldt, J. E. (1958). The rapid diagnosis of ventilatory failure with the carbon dioxide analyser. *Amer. J. Med.*, **25**, 31.

Grollman, A. (1932). *The Cardiac Output of Man in Health and Disease*, p. 13. London: Baillière, Tindall & Cox.

Hackney, J. D., Sears, C. H., and Collier, C. R. (1958). Estimation of arterial CO_2 tension by rebreathing technique. *J. appl. Physiol.*, **13**, 425.

Hubbard, J. P., Preston, W. N., and Ross, R. A. (1942). The velocity of blood flow in infants and young children determined by radioactive sodium. *J. clin. Invest.*, **21**, 613.

Nunn, J. F. (1959). Respiratory measurements in the presence of N_2O; storage of gas samples and chemical methods of analysis. *Brit. J. Anaesth.*, **30**, 254.

Plesch, J. (1909). Hamodynamisch studien. *Zeitschr. f. Exp. Path. u. Therap.*, **6**, 380, pp. 484–499.

Suskind, M., and Rahn, H. (1954). Relationship between cardiac output and ventilation and gas transport, with particular reference to anaesthesia. *J. appl. Physiol.*, **7**, 59.

BOOK REVIEW *continued from page* 255

German surgeon's autobiography. Here is the quotation: "The operation (for a lung condition) was proceeding normally when through a cause we were never able to ascertain, the glowing cautery set light to the ether vapour used as an anaesthetic. The violent explosion which followed was repeated almost immediately as an oxygen cylinder blew up. The patient was killed on the spot, the sister and the assistant were injured and I lost an eardrum." And like King Gama he couldn't think why.

But "Are we wiser better grown"? Anaesthetists have visualized putting us into cold storage and waking us up in a hundred years. What may we find if the experiment is successful? One of the forecasts predicts a European uninhabited and uninhabitable by reason of the fall-out from H-bombs. Our politicians are *talking* about disarmament, but what are they *doing*? Making bigger and better H-bombs, "Blue Streaks", "Black Knights", and many other ingeniously efficient means of destroying us and they call it a method of defence, which it is not, instead of a means of destruction, which it is. This piece of stupidity unless countered will have disastrous consequences which exceed those of the German surgeon's story as millions exceed units.

"The seven foundation stones in order of merit." Is this a task for God or man? Some readers will no doubt be interested in the order of merit according to Dr. Sykes; well here it is.

Rather much space is perhaps given to "The Scottish chloroform legend", of more interest to the student of human nature than to the modern anaesthetist unless perchance he is both, which we will hope he is.

This is a very interesting book which shows the author to be one with an infinite capacity for taking pains.

E. Falkner Hill

Brit. J. Anaesth. (1960), **32**, 262

HALOTHANE AND CIRCULATORY OCCLUSION: SOME EXPERIMENTAL AND CLINICAL OBSERVATIONS

BY

G. R. STIRLING,* K. N. MORRIS,* R. H. ORTON, W. C. BOAKE,†
D. R. RACE,‡ FAY KINROSS, J. W. THOMSON,§ AND W. CROSBY

Alfred Hospital and Baker Medical Research Institute, Melbourne, Australia

THREE aspects of halothane anaesthesia form the basis for this presentation and are discussed separately. The first phenomenon is a fall in blood pressure. Hypotension is not marked in light halothane anaesthesia but as the concentration of halothane is increased more severe hypotension develops. In the opinion of some this results primarily from a direct depression of cardiac activity (Severinghaus and Cullen, 1958). Secondly, halothane has the reputation of reducing cardiac irritability although there have been reports of disturbances of cardiac rhythm during its administration (Chang, Macartney and Graves, 1957). Thirdly, the administration of halothane is associated with a reduction in the body oxygen consumption (Severinghaus and Cullen, 1958).

Reduction in cardiac output and in body oxygen consumption are properties which are common to a number of anaesthetic agents and narcotics (Price and Helrich, 1955). It is probable that much of this reduction is due to the decrease in muscular and respiratory work associated with anaesthesia. The observations on reduced oxygen consumption during halothane anaesthesia prompted us to undertake this work.

The tolerance of an animal to complete circulatory interruption produced by occlusion of both venae cavae is limited by its continuing metabolism, particularly that of the heart and brain. Using standard anaesthetic techniques periods of up to 3 minutes of circulatory occlusion have been used to permit open cardiac operations (Varco, 1957; Lam, 1957; Bjork, 1957). This period may be safely extended by depression of the rate of metabolism with hypothermia and considerable experience with this technique has shown that a period of 8 minutes of circulatory occlusion at 30°C is well tolerated.

A previous communication from this centre (Orton and Morris, 1959) discussed a possible alternative method of prolonging the safe period of circulatory occlusion and presented the early results of the clinical application of deep halothane anaesthesia to open cardiac surgery using inflow occlusion at normal body temperature. This work was based on experimental and clinical observations which suggested that halothane administration was accompanied by a profound reduction in body oxygen consumption.

Claims have been made that at least two other factors are of importance in conferring protection on an animal submitted to circulatory occlusion. The first arose from the work of Crowell, Sharpe, Lambright and Read (1955) from which it was concluded that the administration of heparin to dogs before a period of circulatory arrest would enhance their chances of survival. This conclusion was questioned by Read, Lillehei and Varco (1956) who also pointed out that the incidence of survival and of neurological damage after circulatory occlusion are favourably influenced if the circulation is promptly re-established by vigorous cardiac massage. This would seem self-evident as it results in a total period of ischaemia which is usually much less than that which follows occlusion when massage is not used.

Our investigations are presented in some detail because they have led to a modification of the opinions expressed by some of us in a former publication and because our results differ from those obtained by Read, Lillehei and Varco (1956).

* This work was carried out during the tenure of a research grant from the Life Insurance Medical Research Fund of Australia and New Zealand.
† Alfred Hospital Clinical Research Fellow.
‡ S. W. Jones Medical Research Foundation Scholar.
§ Edward Wilson Memorial Fellow.

I. FACTORS AFFECTING TOLERANCE TO CIRCULATORY OCCLUSION

Method

Eighty dogs, weighing from 5 to 25 kg were used in this study. Premedication always involved the use of atropine sulphate (0.6 mg). Morphine sulphate was added in some experiments in a dose of 1 to 2 mg/kg body weight and, in other experiments, in a dose of 4 mg/kg body weight. Anaesthesia was induced with 2.5 per cent thiopentone, an endotracheal tube was passed and anaesthesia was continued with nitrous oxide and oxygen, in equal amounts, using controlled respiration and a standard soda-lime canister. Occasional small supplements of thiopentone were needed in most experiments. A right thoracotomy was carried out by resecting the fifth rib. The azygos vein was ligated and tapes were passed around the superior and inferior venae cavae and threaded through rubber tubes. The pericardium was widely opened. In some experiments heparin was administered by intravenous injection in a dose of 2 mg/kg body weight or 10 mg/kg body weight 10 minutes before venous occlusion was commenced.

Venous inflow occlusion was effected by traction on the caval tapes. The periods of occlusion varied from 4 to 15 minutes: during this period the respirator was disconnected from the endotracheal tube. At the end of the period of occlusion the respirator was reconnected, the caval tapes were slowly released and, if there was not a prompt rise in arterial blood pressure, cardiac massage was begun. If the tone of the heart muscle was poor after 1 minute of cardiac massage 1 ml of 1 in 20,000 adrenaline was injected into the right atrium. In many cases ventricular fibrillation occurred and electrical defibrillation was necessary. If heparin had been given, protamine sulphate was given to counteract heparin activity, the dose being twice that of heparin.

In some experiments halothane was administered through a vaporiser,* in high concentration up to 4.5 per cent, for 15 to 20 minutes before the cavae were occluded, and this resulted in a fall in arterial blood pressure. When this reached 50 mm Hg halothane was discontinued and venous occlusion was commenced. Halothane was occasionally reintroduced after release of occlusion to lessen hypertension and tachycardia if these developed.

When the circulation had been satisfactorily re-established the chest wound was closed with a drain tube connected to a water seal drainage bottle. Continuous observations of the arterial blood pressure, the electrocardiogram and, occasionally the electroencephalogram were made throughout the experiment.

The 10 dogs submitted to occlusion during hypothermia were anaesthetized with intravenous pentobarbitone in sufficient dosage to control shivering while they were cooled down to an oesophageal temperature between 26.5°C and 30°C by the application of crushed ice in plastic bags. Rewarming was accomplished by the use of a standard laboratory table heater. In 5 dogs an atriotomy was made during the period of circulatory occlusion.

Criteria of Evaluation

(1) If the animal survived the procedure and continued in apparent good health without evidence of cerebral damage it was regarded as having tolerated the period of circulatory occlusion. This is indicated in the accompanying diagram (fig. 1) by an open rectangle placed above the base line.

(2) If the animal died after the procedure, or, if it survived and manifested any signs of severe or permanent neurological damage, then it was regarded as having not tolerated the procedure. These dogs were usually sacrificed during the first 3 days for humanitarian reasons. Both results are represented by a rectangle below the base line. The letters "N" and "C" respectively indicate that the dog survived for a time with evidence of neurological damage or that the dog succumbed from circulatory failure. Neurological damage was assessed clinically from evidence of blindness, ataxia, spasticity or even coma.

Results and Conclusions

A. *Control study* (fig. 1).

Group 1a. Of 7 dogs submitted to 4 minutes of circulatory occlusion without any premedication other than atropine 5 survived the procedure without evidence of neurological damage.

* British Oxygen Co. "Fluothane" vaporizer.

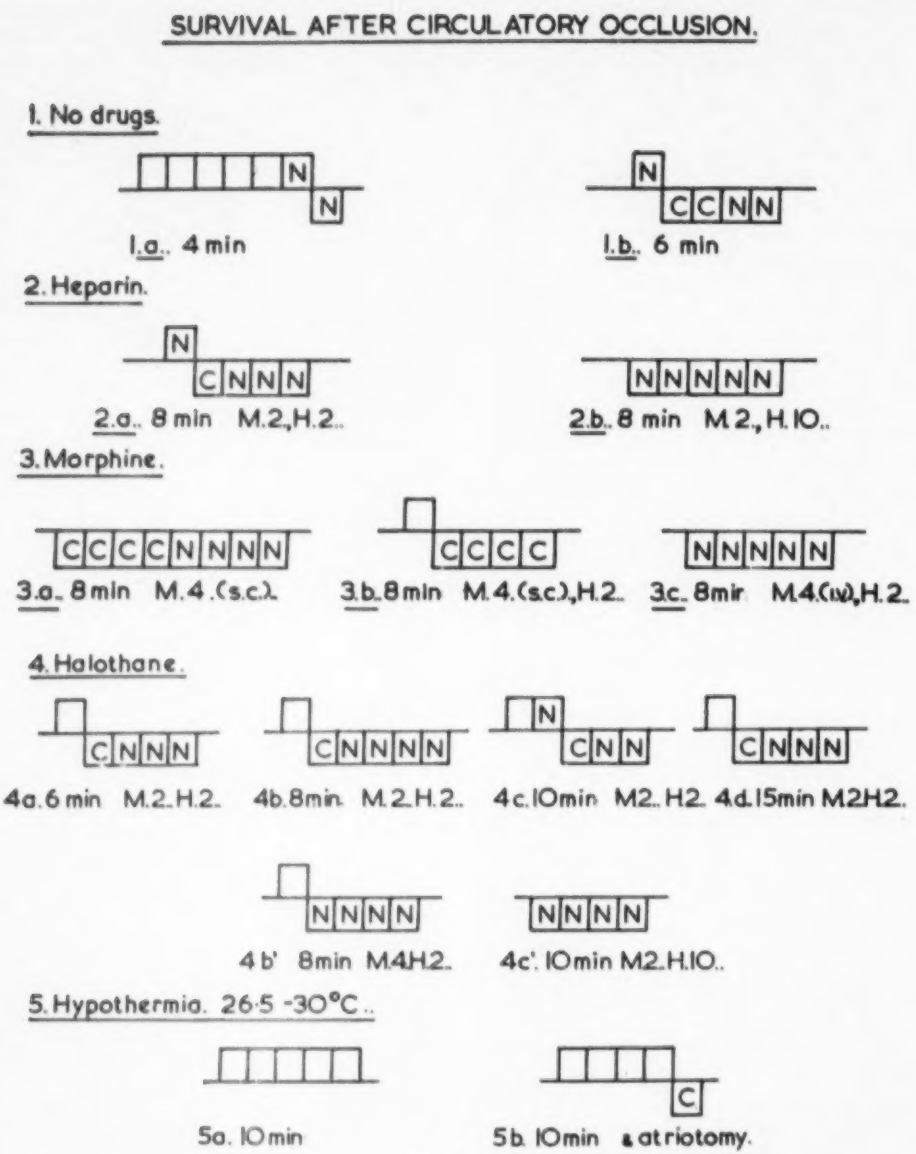


FIG. 1

Schematic representation of occlusion experiments. Rectangles above the base line represent dogs who survived occlusion without evidence of neurological damage. The rectangles below the line represent dogs who died or were sacrificed because of severe neurological damage (N), or circulatory failure (C). M = morphine sulphate; H = heparin. The figures adjacent to these symbols refer to the dose of the drug in mg/kg body weight.

One dog was still blind after 3 weeks and was destroyed and another had impaired vision which recovered after a few days. There was no difficulty in cardiac resuscitation in any of these dogs.

Group 1b. Five dogs were submitted to 6 minutes of circulatory occlusion under similar conditions to those in group 1a. Of these, 1 survived with transient slight neurological damage, 2 survived with severe damage, and were destroyed, and 2 died of circulatory failure.

It is clear that even 4 minutes of circulatory occlusion is not tolerated by all dogs who are not protected by special techniques and that after 6 minutes of occlusion the incidence of severe damage is high.

B. *Effect of heparin* (fig. 1).

Ten dogs were submitted to periods of 8 minutes of circulatory occlusion using morphine sulphate (1 to 2 mg/kg body weight) premedication. Five of these (group 2a) were given heparin in a dose of 2 mg/kg body weight whilst the rest (group 2b) were given heparin in a dose of 10 mg/kg body weight. None of these 10 dogs survived without stigmata of neurological damage. This series of experiments was prompted by the observations of Crowell, Sharpe, Lambright and Read (1955) which led them to consider that heparin would protect an animal under the conditions of circulatory arrest. We cannot support this view and would agree with the conclusions of Read, Lillehei and Varco (1956) that heparin has no significant protective effect. Read, Lillehei and Varco also state that "interference with the circulation for 8 minutes resulted in 1 out of 18 dogs showing persistent brain damage"; it is clear that our results are in marked contrast to theirs.

We consider that a possible factor of significance was the high dose of morphine sulphate (4 mg/kg body weight) used by Read and his colleagues in their experiments.

C. *Effect of morphine sulphate* (fig. 1).

Group 3a. Eight dogs failed to recover completely from 8 minutes of circulatory occlusion when morphine sulphate was administered subcutaneously as pre-anaesthetic medication in a dose of 4 mg/kg body weight.

Group 3b. One dog, of a group of 5, survived 8 minutes of circulatory occlusion after pre-anaesthetic medication with morphine sulphate (4 mg/kg body weight) and the administration of heparin (2 mg/kg body weight).

Group 3c. Five dogs were given an intravenous injection of morphine sulphate (4 mg/kg body weight) 5 minutes before they were submitted to 8 minutes of circulatory occlusion. In all a profound hypotension resulted and, although they all survived the procedure, all manifested severe signs of neurological damage.

We were therefore unable to reproduce the results of Read, Lillehei and Varco, and were unable to demonstrate that morphine sulphate conferred significant protection on dogs submitted to 8 minutes of circulatory occlusion.

D. *Effect of halothane.*

Orton and Morris (1959), on the basis of certain theoretical considerations and a small laboratory experience, suggested that halothane, by reducing the metabolic rate, might protect animals from damage during circulatory occlusion. The results of thirty experiments in which the halothane-heparin technique has been used are presented in figure 1.

In these experiments, except where indicated, the dogs received pre-anaesthetic medication with morphine sulphate (1 to 2 mg/kg body weight) and were given heparin (2 mg/kg body weight) 10 minutes before venous occlusion for periods of 6, 8, 10 and 15 minutes (groups 4a, 4b, 4c, 4d).

Certain observations of interest were made during these experiments. Spontaneous ventricular fibrillation was encountered on only two occasions. The general pattern was that after 6 to 10 minutes of occlusion the heart rate slowed markedly and finally atrioventricular dissociation occurred. In 3 of 5 dogs occluded for 15 minutes (group 4d) asystole occurred after 11 to 12 minutes.

Cardiac resuscitation was usually possible but most of the surviving dogs showed evidence of severe neurological damage and were destroyed. As can be seen from the figure there were isolated survivors, without evidence of neurological damage after periods of occlusion of 6, 8, 10 and 15 minutes. Unfortunately these occurred preponderantly in our early laboratory experience.

If groups 4b and 4c are studied it is clear that increasing the morphine dosage to 4 mg/kg body weight or the heparin dosage to 10 mg/kg body weight made no significant difference to these results.

Finally it should be clearly stated that the halothane-heparin technique does not confer sufficient protection to make occlusion of the dog's circulation for 6 minutes a safe procedure.

E. *Effect of hypothermia.*

The tolerance of experimental animals to circulatory occlusion under conditions of hypothermia is far better documented than is the tolerance of the same animals to occlusion at normal temperatures. We do not wish to add to this already voluminous literature.

In our laboratory occlusion of the dog's circulation for 10 minutes at 26.5°C to 30°C was well tolerated by 5 dogs (group 5a) and 4 of 5 dogs who were occluded for 10 minutes, during which time an atriotomy was performed, also survived (group 5b).

Clinical Experiences

The technique and results of the first 14 patients operated on with the halothane-heparin technique were reported by Orton and Morris (1959). Twenty-eight patients have now undergone direct vision open heart surgery using this technique.

Valvular pulmonary stenosis.

In 11 cases of pure valvular pulmonary stenosis there have been no deaths. The times of circulatory occlusion have ranged from 1 min 45 sec to 2 min 40 sec.

In one case of pulmonary stenosis associated with hypoplasia of the right ventricle and atrial septal defect death occurred suddenly 18 hours after operation. The pulmonary stenosis had been inadequately relieved and the atrial septal defect had been completely closed. This patient had his circulation occluded for 5 min 15 sec. He demonstrated no clinical or pathological stigmata of neurological damage.

Aortic stenosis.

Thirteen cases of aortic stenosis have been submitted to open operation using this technique. The periods of occlusion ranged between 1 min 45 sec and 3 min 15 sec. Three children with congenital aortic stenosis have already been cited by Orton and Morris (1959). The remaining 10 cases have been adults with calcified aortic stenosis. There have been 3 deaths in this group. We have attributed death to inadequate relief of the aortic stenosis in 2 of these cases and to the creation of aortic incompetence in the third. Nicks of Sydney (1959) has reported successful results in operations on 13 of 14 cases of aortic stenosis.

Atrial septal defect.

Three cases of atrial septal defect have been submitted to operation using the halothane-heparin technique. Two of these have been described in detail in an earlier publication. Our experience with the third case detailed below has caused us to reverse the opinion expressed by Orton and Morris (1959)—"it is considered that, under these circumstances, periods of circulatory arrest of at least 5 minutes, and probably longer, can be achieved with safety."

J.B., a 17-year-old girl had the typical features of an atrial septal defect with a large left to right shunt. This was confirmed by cardiac catheterization. She was submitted to open operation for closure of the atrial septal defect using the halothane-heparin technique during which her circulation was occluded for 5 min 15 sec. A typical foramen ovale type of defect was found and closed by direct suture. The operation was uneventful but on recovery from the anaesthetic the patient manifested signs of cerebral irritation which persisted for 12 hours. She then made a prompt and complete recovery from this episode and left hospital 3 weeks later with no evidence of neurological damage and with signs suggesting that her atrial septal defect was completely closed. Despite the successful end result we feel that this experience was a salutary indication that, under these circumstances, 5 minutes must be regarded as the upper limit of tolerance to circulatory occlusion in the normothermic human subject.

II. THE CIRCULATORY EFFECTS OF HALOTHANE

The administration of moderate to high concentrations of halothane to man or dog is accompanied by a progressive fall in systemic arterial blood pressure. Two series of experiments were carried out in order to determine whether this hypotension resulted from cardiac depression or from peripheral vasodilatation or both.

Right Ventricular Performance During the Administration of Halothane

Method.

Six dogs, the weights of which ranged from 15 to 20 kg, were used in this study. Premedica-

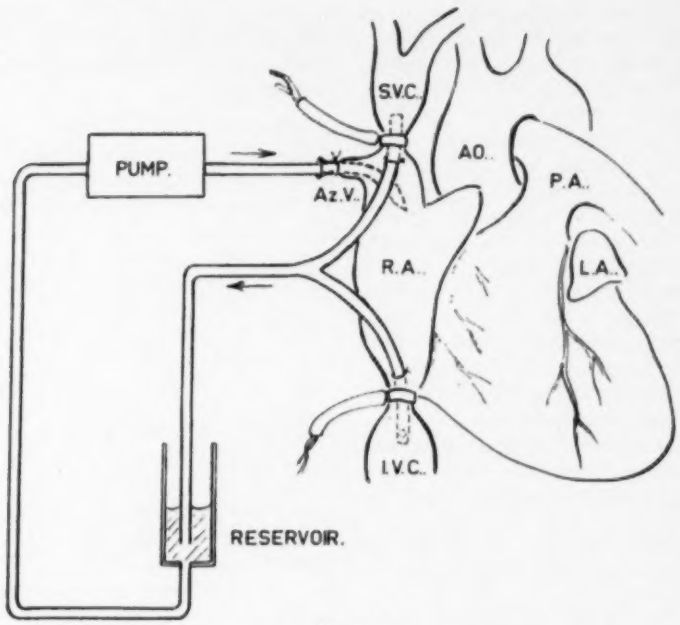


FIG. 2

Experimental arrangement used for study of right ventricular function. Venous blood siphoned from both venae cavae (S.V.C., I.V.C.) drains into a reservoir which is emptied at a series of known rates of flow by a pump which returns the blood to the right atrium (R.A.) through a cannula introduced through the azygos vein (Az.V). Pressures are continuously recorded from the right atrium and the pulmonary artery (P.A.).

tion consisted of morphine sulphate (1 mg/kg body weight) and atropine sulphate (0.6 mg). Anaesthesia was induced with thiopentone and continued using nitrous oxide and oxygen in equal amounts with constant volume positive pressure ventilation through an endotracheal tube. Small supplements of thiopentone were used during the course of the experiment. The right pleural cavity was opened by excising the fifth rib. The azygos vein was then dissected free and tapes were passed around the superior and inferior venae cavae. The pericardium was widely opened and two wide-bore cannulae were introduced through the atrial appendage. These were guided into the superior and inferior venae cavae respectively whilst a third shorter cannula was introduced through the azygos vein and directed into the cavity of the right atrium (fig. 2). The two caval cannulae were used to siphon the returning venous blood to a reservoir which, in turn, was emptied by a pump which propelled the blood through the inflow cannula back into the right atrium. When the tapes around the cavae were tightened snugly around the cannulae the whole of the venous return to the heart, with the exception of the coronary return, was forced to traverse this extracorporeal circuit. Before each experiment the pump* was carefully calibrated to produce a series of known rates of flow which ranged from 40 ml/kg/min to 200 ml/kg/min. It has been found that these flows are reproducible with an error of less than 5 per cent. In other words, a preparation was constructed which enabled the operator to present the intact dog's heart with a graded series of known rates of

* Sigmamotor T.6S. Sigma Motor Inc., Middleport, New York.

cardiac inflow. Fine polyethylene catheters were introduced into the right atrium, the pulmonary artery and the aorta and these were connected to Cambridge electromanometers. Full pulse tracings and electronically integrated mean pressures were continuously monitored and recorded whilst the rate of cardiac inflow was changed by adjustment of the pump to a series of predetermined rates. The pressure readings used in the calculations were those obtained after the system had reached equilibrium following a change in flow rate. This was evidenced by stable pressures and a constant volume in the venous reservoir. In most experiments equilibrium was reached 2 minutes after a change in rate of inflow. Care was taken to ensure that tricuspid regurgitation was not present by constant reference to a fast pulse tracing. The pressure responses to at least five different rates of inflow were used to construct a "control" right ventricular function curve.

At this stage the preparation was maintained at a constant flow rate and a halothane vaporizer* was fitted into the anaesthetic circuit so that concentrations of 0.5 to 2.5 per cent halothane could be added to the nitrous oxide and oxygen mixture. After 15 minutes of halothane administration a stable situation was reached and a further series of pressures was recorded in response to the same graded series of rates of cardiac inflow. From these data a second right ventricular function curve was constructed and compared with the control curve.

Right ventricular minute work was calculated from the following formula:

$$W\ min = \frac{(P.P.A. - P.R.A.)F}{100}$$

where W min = minute-work of right ventricle (gram-metres)

P.P.A. = mean pulmonary artery pressure (cm water)

P.R.A. = mean right atrial pressure (cm water)

F = minute volume (ml)

It should be noted that the coronary venous return to the right atrium has not been included in the minute volume, nor has the accleration component of right ventricular work been included in the calculations (Sarnoff and Berglund, 1954).

Results.

The results of these experiments are presented as right ventricular function curves which relate the minute work of the right ventricle to its filling pressure or mean atrial pressure. The normal curve is found to be almost a straight line with a steep gradient (Stirling, Stanley and Lillehei, 1957). Impairment of right ventricular function is indicated by a shift of the curve to the right and by a flattening of the curve at higher right atrial pressures. Consistent results were obtained in all six experiments and two examples of these are illustrated in figure 3. In all cases the administration of halothane resulted in an impairment of right ventricular function. The degree of impairment was proportional to the concentration of halothane in the ventilating gases. When concentrations of greater than 1.5 per cent were used the impairment of ventricular function was severe.

The Effects of Halothane Administration on the Peripheral Circulation.

Awareness of the depressant effect of halothane on ventricular performance prompted us to design experiments in which the cardiac and peripheral actions of halothane could be divorced.

Method.

In a series of three experiments the preparation already described for the study of right ventricular function was used to submit a dog to a constant rate of cardiac inflow (100 ml/kg/min).

Mean pressures in the aorta, pulmonary artery and right atrium were continuously recorded. After a period of 15 minutes, during which the dog was ventilated with nitrous oxide and oxygen in equal proportions, halothane was introduced into the gas mixture and its concentration rapidly increased to 2 per cent. A steadily progressing fall in mean aortic pressure was observed and this was accompanied by a progressive rise in the mean pressures in the pulmonary artery and right atrium. The results of one of these experiments are illustrated in figure 4. It is assumed, but not established, that the cardiac output was main-

* British Oxygen Company "Fluothane" Vaporizer. The authors do not wish to infer that the concentrations referred to in this text are absolutely accurate.

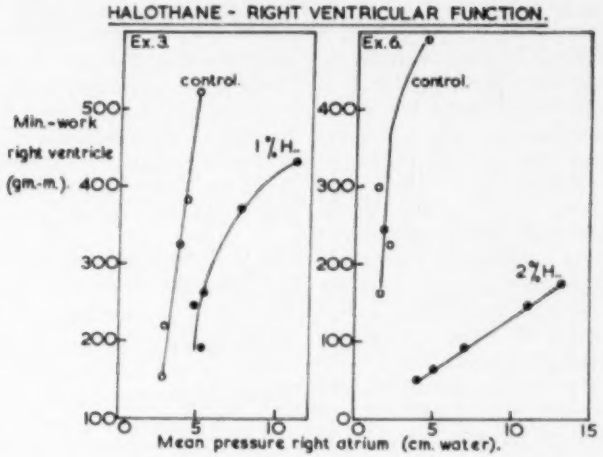


FIG. 3

Right ventricular function curves obtained during the administration of halothane in concentrations of approximately 1 per cent (left) and 2 per cent (right). Both curves, when compared with their respective control curves show significant impairment of ventricular function.

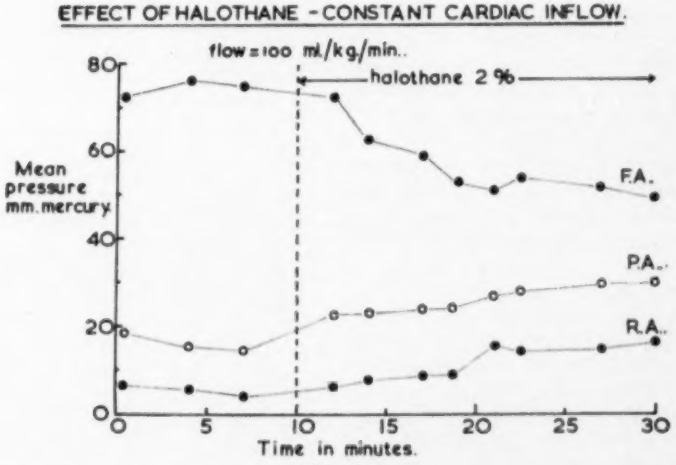


FIG. 4

Changes in pressure recorded in the femoral artery (F.A.), pulmonary artery (P.A.) and right atrium (R.A.) before and during the administration of 2 per cent halothane to a dog with a fixed rate of cardiac inflow of 100 ml/kg body weight/min.

tained constant during this experiment and therefore that the changes in aortic pressure reflect a progressive fall in systemic vascular resistance.

In another series of experiments involving 5 animals total cardiopulmonary bypass was established in the standard fashion using a rotating disc type of oxygenator* and sigmamotor pumps. The perfusion rate for each dog was kept constant throughout the experiment but the rates of flow used in the five experiments varied from 50 to 108 ml/kg body weight/min. The ventilating gas in the oxygenator consisted of 95 per cent oxygen and 5 per cent carbon dioxide and was delivered at a rate of 10 l./min. A halothane vaporizer was inserted in the gas line to the oxygenator but halothane was not administered until the animal had been on bypass for 15 to 20 minutes and had been in a stable state for at least 10 minutes.

Commonly the aortic pressure and the volume in the extracorporeal circuit stabilized after 5 to 8 minutes. During this stable period samples of arterial and venous blood were taken from the lines of the oxygenator for determination of oxygen content by the method of Peters and Van Slyke.

Halothane was then introduced with the ventilating gases into the cylinder of the oxygenator and serial measurements of the aortic blood pressure and the volume in the extracorporeal circuit were made. After a period of 15 to 20 minutes of halothane administration further blood samples were taken for oxygen determination. Halothane was then discontinued and after a further 20 minutes further blood samples were taken.

Results

In all experiments the administration of halothane resulted in a progressive fall in aortic pressure and a progressive fall in the volume of blood in the extracorporeal circuit. The significance of the former observation is that halothane caused a fall in systemic vascular resistance; the latter observation indicates that the volume of blood in the dog increased during halothane administration but gives no indication of the distribution of the blood in the animal. When halothane was discontinued these parameters returned to the control levels in a period of 10 to 15 minutes. Figure 5 is an illustration of the blood pressure changes in a typical experiment.

It was concluded from these experiments that halothane, when administered in high concentration, produces a profound depression of ventricular function and also a profound reduction in systemic vascular resistance.

III. THE EFFECT OF HALOTHANE ON THE OXYGEN CONSUMPTION OF THE DOG DURING TOTAL CARDIOPULMONARY BYPASS

Severinghaus and Cullen (1958) observed that the induction and maintenance of anaesthesia with halothane in human subjects was accompanied by a reduction in total body oxygen consumption. The factors responsible for this are many and include reduced respiratory, muscular and cardiac activity. To exclude these variables, in an attempt to determine the effect of halothane on the rate of metabolism of the body tissues in general, a series of five experiments was undertaken in which the total body oxygen consumption of the dog, under the circumstances of total cardiopulmonary bypass, was determined before, during and after the addition of halothane to the ventilating gases of the oxygenator. The experimental method has already been described in the previous section.

The oxygen consumption of an animal during bypass is influenced by a number of factors. Two of these, blood flow rate and temperature, were carefully controlled during these experiments. Oxygen consumptions were calculated using the Fick principle; the flow rate was controlled at a known level and the arteriovenous oxygen differences were measured. The results are presented in table I. For purposes of com-

TABLE I

Expt. no.	Flow ml/kg/min	Oxygen consumption ml. O_2/kg body weight/min		
		Before halothane	During halothane	After halothane
283	50	3.6	3.3	3.2
399	60	4.4	4.4	5.9
295	65	4.4	6.0	5.9
358	100	4.1	4.2	4.1
367	108	6.5	6.1	—
Mean		4.8	4.8	4.5

* Kay-Cross oxygenator. Pemco Inc., Cleveland, Ohio.

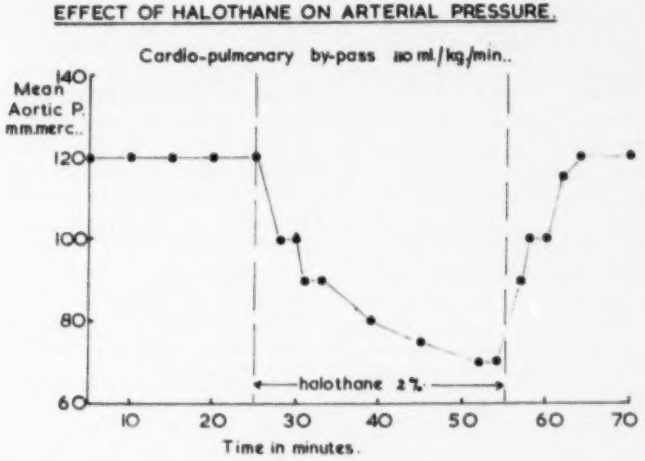


FIG. 5

Changes in aortic pressure of a dog on total cardiopulmonary bypass before, during and after the administration of 2 per cent halothane. The perfusion was maintained at a constant level of 110 ml/kg body weight/min.

parison the results have been expressed in terms of millilitres of oxygen consumed per minute per kilogram of body weight. They reveal no consistent and significant effect of halothane administration on the oxygen consumption of the dog during cardiopulmonary bypass.

DISCUSSION

Unsupported circulatory occlusion is now an established technique allowing direct vision intracardiac surgery. Curiously the limits of tolerance of both the experimental animal and the human subject to circulatory occlusion under the circumstances of general hypothermia have been extensively investigated and well documented whilst tolerance at normal body temperature is less well defined. The basic hypothesis that the time of permissible circulatory occlusion is inversely proportional to the metabolic rate, is now fairly well established. Thus, while the limit of permissible circulatory occlusion at a body temperature of 38°C is probably about 4 minutes, lowering the temperature to 30°C allows this time to be doubled at least. At present the induction of general hypothermia seems to be the only practical technique whereby the resting metabolic rate of the anaesthetized subject may be significantly lowered. We must look to the researches of the biochemist and the pharmacologist for alternative methods of achieving this end.

The attraction of techniques of venous inflow occlusion lies in their relative simplicity whilst their main disadvantage lies in the fact that the time of the intracardiac procedure is strictly limited. Their beneficial application to intracardiac surgery is dependent on the exhibition of sound surgical judgment based on experience which has been intelligently interpreted.

We have found the clinical technique described by Orton and Morris (1959) to be satisfactory, enabling the surgeon to perform pulmonary or aortic valvotomy. Indeed three cases of atrial septal defect have been successfully managed by this technique although this is no longer recommended for the reasons already stated in detail.

The factors in this success proved difficult to evaluate. We have demonstrated in the laboratory animal that neither halothane nor heparin nor morphine has any marked effect in prolonging the safe period of circulatory occlusion. Although halothane effects a reduction in total body oxygen consumption, it does not appear to

produce this by any specific action other than the reduction in cardiac, respiratory and muscular work which follows the induction of deep anaesthesia. The attractive hypothesis of Crowell et al. (1955) that the damage incurred during circulatory occlusion may result, in part, from intravascular thrombosis during circulatory stasis receives no support from our work although, on a priori grounds, it would seem reasonable to administer heparin before circulatory occlusion if this is not attended by any increased morbidity. Clearly an important factor in our success has been that human tolerance to circulatory occlusion at normal body temperature has been underrated.

The hypotension which accompanies deep halothane anaesthesia has been of inestimable value during the performance of aortic valvotomy. The side excluding clamp is applied to a relatively flaccid aorta before valvotomy is carried out. After valvotomy, when the clamp is reapplied, the aortic blood pressure may be rapidly controlled by the exhibition of further halothane should hypertension develop following circulatory occlusion. We feel that this endows the technique with a considerable safety factor. Apart from these technical considerations it is possible that moderate hypotension immediately following circulatory occlusion is, in itself, beneficial in so far as the potential work load of the heart is reduced.

SUMMARY

Some of the factors affecting the tolerance of the dog to circulatory occlusion at normal temperature have been studied.

The limit of safe circulatory occlusion in the dog was found to be less than 4 minutes.

The administration of morphine and of heparin did not significantly prolong the safe period of occlusion.

The use of the halothane and heparin technique did not significantly improve the results, although occasional survivals after periods of up to 15 minutes of occlusion were obtained.

The hypotension of deep halothane anaesthesia has been analyzed. It was found that halothane produces a depression in ventricular function and also results in a profound reduction in systemic vascular resistance.

Halothane was found to have no significant effect on the oxygen consumption of the dog during total cardiopulmonary bypass.

The use of circulatory occlusion for open heart surgery at normal body temperature is discussed in relation to a clinical experience with 28 cases using the halothane-heparin technique.

ACKNOWLEDGMENTS

We are grateful to Dr. T. E. Lowe, Director of the Baker Medical Research Institute, for valuable advice and encouragement during the conduct of these investigations.

I.C.I. of Australia and New Zealand kindly supplied us with all the Fluothane used in this study.

REFERENCES

Bjork, V. O. (1957). Personal communication.

Chang, J., MacCartney, H., and Graves, H. B. (1957). Clinical experience with Fluothane, A new non-explosive anaesthetic agent. *Canad. Anaesth. Soc. J.*, **4**, 187.

Crowell, J. W., Sharpe, G. P., Lambright, R. L., and Read, W. L. (1955). The mechanism of gas after resuscitation following acute circulatory failure. *Surgery*, **38**, 696.

Lam, C. (1957). Personal communication.

Nicks, R. (1959). Personal communication.

Orton, R. H., and Morris, K. N. (1959). Deliberate circulatory arrest. The use of halothane and heparin for direct-vision intra-cardiac surgery. *Thorax*, **14**, 39.

Price, H. L., and Helrich, M. (1955). Effect of cyclopropane, diethyl ether, nitrous oxide, thiopental, and hydrogen ion concentration on myocardial function of the dog heart-lung preparation. *J. Pharmacol. exp. Ther.*, **115**, 206.

Read, R. C., Lillehei, C. W., and Varco, R. L. (1956). Cardiac resuscitation and neurologic tolerance to anoxia. *Circulat. Res.*, **4**, 45.

Sarnoff, S. J., and Berglund, E. (1954). Ventricular function. (1) Starling's law of the heart studied by means of simultaneous right and left ventricular function curves in the dog. *Circulation*, **9**, 706.

Severinghaus, J. W., and Cullen, S. C. (1958). Depression of myocardium and body oxygen consumption with Fluothane. *Anesthesiology*, **19**, 165.

Stirling, G. R., Stanley, P. H., and Lillehei, C. W. (1957). The effects of cardiac by-pass and ventriculotomy upon right ventricular function; with report of successful closure of ventricular septal defects by use of atriotomy. *Surg. Forum*, **8**, 433.

Varco, R. L. (1957). The electroencephalogram in patients undergoing open intra-cardiac operation with the aid of extra-corporeal circulation. In discussion on—Muller, W. H., and Longmire, W. J. jr. (1951). *J. Thorac. Surg.*, **34**, 709.

Brit. J. Anaesth. (1960), **32**, 273

A NOTE ON THE RESPIRATORY EFFECTS OF ANILERIDINE

BY

MARK SWERDLOW

Salford Royal Hospital, Manchester, England

ANILERIDINE dihydrochloride has been shown to be a useful analgesic agent for pre-operative medication (Dechene and Hebert, 1959), post-operative medication (Riffin et al., 1958; Dechene and Hebert, 1959) and for the supplementation of anaesthesia (Chang, Safar and Lasagna, 1958; Swerdlow, Brown and Tetlow, 1960). The present paper reports a small study of the effects of anileridine on respiration in anaesthetized subjects. The results are compared with those of an investigation of the respiratory effects of pethidine, carried out earlier under identical conditions (Swerdlow, 1957). The standard of equipotency adopted was that of Keats, Kurosu and Telford (1957), i.e. 40 mg anileridine is equivalent to 100 mg pethidine. As a dose of 0.6 mg/kg pethidine had been employed in the pethidine study (Swerdlow, 1957) the dose of anileridine used initially in the present work was therefore 0.24 mg/kg.

EXPERIMENTAL TECHNIQUE

The experimental conditions employed have been described in detail elsewhere (Swerdlow, 1957, 1959). Briefly, the premedicated patient was given 8 mg/kg 5 per cent thiopentone sodium by intravenous injection in 45 seconds. Nitrous oxide and oxygen were then administered and 5 minutes after the start of the thiopentone injection the respiration rate and minute volume were measured. At 6 minutes 0.24 mg/kg anileridine dihydrochloride was injected intravenously in 15 seconds and the respiratory rate and minute volume were measured 3, 5, 7 and 9 minutes later (i.e. 9, 11, 13 and 15 minutes after "zero"). Respiratory volume was measured with a Bennett ventilation meter inserted on the expiratory side of the circuit. All the patients were aged between 18 and 60 years and were in good general condition.

In view of the effects of this dose of anileridine a further group of 20 patients were given half the above dose of the narcotic (i.e. 0.12 mg/kg) under similar conditions and the same measurements were made.

RESULTS

Anileridine 0.24 mg/kg

Of the 20 patients who were given 0.24 mg/kg anileridine, 7 developed apnoea which lasted from 7 to 15 minutes. (During this period the respirations were assisted by gentle squeezing of the breathing bag.) None of the patients in the (earlier) pethidine series developed apnoea. The mean percentage changes in respiratory rate and volume are shown in tables I and II, together with the comparable figures for the pethidine series. It will be seen that this dose of anileridine produced significantly more depression of the respiration than 0.6 mg/kg pethidine.

TABLE I

Respiration rate

Percentage change from control (means of individual deviations)

Drug	9 min	11 min	13 min	15 min	Student's t	Significance P
Pethidine	−48.0	−53.5	−53.3	−52.0	—	—
Anileridine 0.12 mg	−41.8	−44.8	−45.1	−44.3	2.5796	$.01<P<0.02$
Anileridine 0.24 mg	−74.3	−75.4	−76.7	−73.5	6.8463	$P<0.001$
Anileridine 0.24 mg (excluding apnoeic cases)	−62.4	−64.1	−61.9	−60.2	3.5857	$P<0.001$

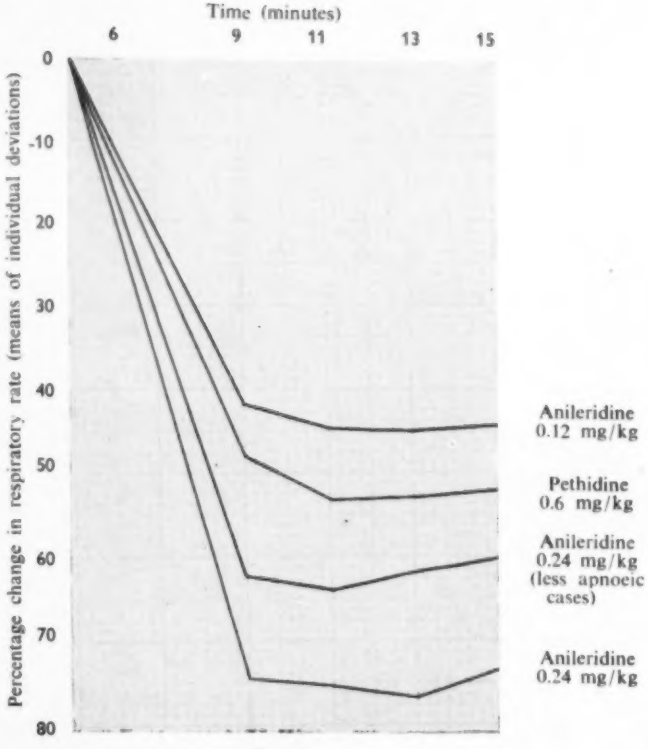

Time (minutes)
6
9
11
13
15
0
-10
20
30
40
50
60
70
80
Percentage change in respiratory rate (means of individual deviations)
Anileridine 0.12 mg/kg
Pethidine 0.6 mg/kg
Anileridine 0.24 mg/kg (less apnoeic cases)
Anileridine 0.24 mg/kg

FIG. 1

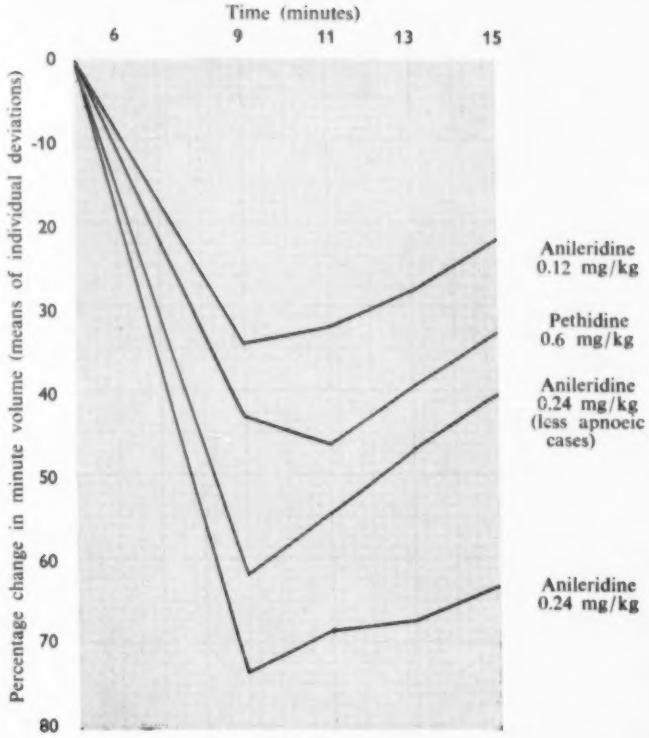

Time (minutes)
6
9
11
13
15
0
-10
20
30
40
50
60
70
80
Percentage change in minute volume (means of individual deviations)
Anileridine 0.12 mg/kg
Pethidine 0.6 mg/kg
Anileridine 0.24 mg/kg (less apnoeic cases)
Anileridine 0.24 mg/kg

FIG. 2

TABLE II

Minute volume

Percentage change from control (means of individual deviations)

Drug	9 min	11 min	13 min	15 min	Student's t	Significance P
Pethidine	−43.4	−46.2	−39.5	−33.5	—	—
Anileridine 0.12 mg	−34.5	−32.4	−28.3	−22.0	3.6910	P<0.001
Anileridine 0.24 mg	−74.0	−69.0	−67.6	−63.6	7.0583	P<0.001
Anileridine 0.24 mg (excluding apnoeic cases)	−61.9	−54.7	−46.9	−40.4	3.2615	P<0.01

Anileridine 0.12 mg/kg.

This dose of anileridine did not give rise to apnoea in any patient. Statistical analysis shows that 0.12 mg/kg anileridine caused significantly less depression of the minute volume than did 0.6 mg/kg pethidine and appreciably less depression of the respiratory rate (see tables I and II). The results are shown in graphic form in figures 1 and 2.

In conclusion, in terms of its effects on respiration, anileridine has been found to be between 2.5 and 5 times as potent as pethidine. This is similar to the analgesic potency ratio (3.8:1) which was found in a clinical comparison of anileridine and pethidine (Swerdlow, Brown and Tetlow, 1960).

ACKNOWLEDGMENTS

I am grateful to Miss Marion H. Russell, Medical Statistician, Christie Cancer Hospital, Manchester, for carrying out the statistical analysis of the results.

REFERENCES

Chang, F. F. C., Safar, P., and Lasagna, L. (1958). Narcotic potency and side effects of anileridine and meperidine in man. *J. Pharmacol.*, **122**, 370.

Dechene, J.-P., and Hebert, C. (1959). Anileridine: a new synthetic analgesic in anaesthesia. *Canad. Anaesth. Soc. J.*, **6**, 393.

Keats, A. S., Kurosu, Y., and Telford, J. (1957). Studies of analgesic drugs: anileridine dihydrochloride. *Anesthesiology*, **18**, 690.

Riffin, I., Wheaton, H. H., Schwarz, B., Preisig, R., and Landman, M. (1958). Anileridine: an evaluation of its use in anesthesia and in postoperative analgesia. *Curr. Res. Anaesth.*, **37**, 154.

Swerdlow, M. (1957). The respiratory effects of pethidine and levallorphan. *Anaesthesia*, **12**, 174.

—— (1959). The duration of action of levallorphan. *Anaesthesia*, **14**, 178.

—— Brown, P. B., and Tetlow, A. (1960). Anileridine in anaesthesia: a clinical trial. *Anaesthesia* (in press).

Brit. J. Anaesth. (1960), **32**, 276

A STUDY OF HYPOTENSIVE ANAESTHESIA IN THE ELDERLY

BY

W. N. ROLLASON

The Royal Infirmary, Aberdeen, Scotland

AND

J. M. HOUGH

The University, Hull, England

As part of a general investigation (Rollason and Hough, 1960) of the importance of age as a contra-indication to hypotensive anaesthesia, it was decided to make a clinical study under controlled conditions. The work of Debenham and Ward (1960) suggested that retropubic prostatectomy would be an ideal operation for such a study because the employment of hypotensive anaesthesia may permit the omission of an indwelling catheter, and such patients are usually elderly.

The hypotensive series was compared with a larger group of cases operated on under normotensive anaesthesia.

MATERIAL AND METHODS

In the main investigation, 40 unselected patients having a retropubic prostatectomy under hypotensive anaesthesia were studied.

Pre-operatively, and several weeks postoperatively, the patient's blood urea, serum bilirubin, teleradiogram and e.c.g picture were examined.

Before, during and after the surgical procedure, the blood pressure, pulse rate and e.c.g. (recorded on a Cambridge direct writer) were observed. Standard leads I, II and III and precordial lead V5 were routinely used.

The hypotensive technique employed varied as follows:

Epidural block using 1.5 per cent lignocaine	19 cases
Ganglionic blockade using trimetaphan or trophenium by continuous drip	12 cases
Subarachnoid block using 1/200 cinchocaine	8 cases
Halothane	1 case

As an e.c.g. was not available, the effects of any cerebral ischaemia produced were investigated clinically by interrogating the patient and, when possible, the relatives as well.

The patients were classified as A, B, or C risks; A risks were clinically healthy; B risks had either pulmonary or cardiac pathology; C risks had both. In addition, cases with a history of cerebral or coronary damage were classified as C risks.

The age and grade of risk for the patients submitted to hypotension are listed in table I. The duration of the low pressure phase taken as the period for which the systolic blood pressure was below 80 mm Hg is also shown. The exact lesion in cases of known cardiovascular disease in the series is shown in table II.

In order to compare the morbidity and mortality with normotensive techniques, the records for prostatectomies in the same hospital over a period of 4–5 years were studied. In this series of 103 cases, e.c.g. tracings and laboratory tests were not performed and consequently only information on mortality and the grosser forms of morbidity were available.

MORTALITY

The causes of death in the fatal cases in the hypotensive series are recorded in table III and those for the normotensive group in table IV. In case No. 25, the patient died after the induction of anaesthesia during the preliminary cystoscopy; unfortunately the e.c.g. machine was disconnected at this time while the operating table was being moved for the preliminary investigation.

The mortality for the two series is compared in table V. Analysis of statistical significances in these figures is impossible owing to the small numbers involved. Table III shows that only in case No. 25 could it be suggested that hypotension was a likely cause of death. The postmortem report in this case revealed a haemorrhagic myocardial infarction, implying that the infarction

TABLE I

Case No.	Age	Grade of risk	B.P. (mm Hg)		Pulse rate		Duration of low pressure in minutes
			Pre-op.	Lowest pressure	Pre-op.	Average during low pressure phase	
1	72	B	140/80	55/40	75	70	90
2	72	B	230/105	50/35	85	85	90
3	63	A	140/80	80/60	75	75	30*
4	78	B	160/100	50/35	105	95	60
5	64	C	170/105	60/40	85	70	90
6	69	B	145/90	60/45	70	70	85
7	75	B	170/70	60/45	75	70	50
8	64	C	220/120	125/90	75	85	60*
9	65	B	180/100	65/50	60	70	50
10	72	A	150/75	65/45	95	75	50
11	72	A	145/70	80/65	75	75	30*
12	73	A	130/80	70/50	85	105	15
13	64	A	160/100	60/40	75	75	25
14	70	B	180/110	70/50	80	85	40
15	67	B	200/130	55/40	85	85	35
16	75	B	210/140	90/70	75	75	80*
17	64	A	110/70	80/40	80	65	70
18	71	C	210/130	50/35	85	80	75
19	73	C	210/90	50/30	85	85	80
20	71	B	180/85	45/30	95	75	75
21	61	A	150/90	60/45	80	60	45
22	63	B	180/90	55/40	85	60	75
23	53	A	160/100	55/35	80	60	50
24	70	C	250/150	50/35	80	65	70
25	75	C	210/115	45/30	80	140	20 D.O.T.
26	72	C	150/80	55/35	60	50	55
27	59	B	140/80	70/50	80	75	60
28	76	C	195/90	50/30	75	55	70
29	71	B	210/90	50/35	65	70	55
30	71	B	210/100	45/30	70	60	30
31	74	B	140/85	55/35	80	85	55
32	74	A	140/80	60/40	85	75	80
†33	78	B	130/90	80/55	70	65	5*
34	74	B	105/65	60/45	80	70	60
35	78	B	140/90	50/30	75	85	25
36	80	C	125/80	55/35	95	85	70
37	76	B	180/100	60/50	80	60	50
38	83	B	165/100	50/35	85	50	70
39	64	C	160/90	45/35	85	70	80
40	85	B	155/90	60/40	95	50	70

* Time systolic pressure below 2/3 pre-operative systolic pressure.
† Case received a vasopressor.

TABLE II

Patients with known cardiovascular disease

Case No.	Type of disease
5	Angina of effort
8	Old coronary infarct and cerebral thrombosis
24	Left ventricular hypertrophy
25	Old coronary infarct
26	Old coronary infarct
36	Left ventricular hypertrophy

probably started prior to the induction of anaesthesia.

Debenham and Ward (1960), Griffiths (1959), and Bodman (1960) have also investigated mortality following prostatectomy under hypotensive anaesthesia. The first workers had a mortality of 10 in 259 cases (approximately 4 per cent) using the combined "lytic cocktail" and spinal technique. Griffiths had a mortality of 22 per cent in 120 cases under normotensive anaesthesia and a mortality of 8 per cent in 115 cases under

TABLE III

Mortality in the hypotensive series

Case No.	Time of death after operation	Cause of death
16	4th day	Uraemia due to lower nephron nephrosis and broncho-pneumonia
19	19th day	Bronchopneumonia
25	D.O.T.	Cardiac arrest due to myocardial infarction
38	5th day	Uraemia secondary to clot retention

TABLE IV

Mortality in the normotensive series

Grade of risk	Case No.	Time of death after operation	Cause of death
A	31	40th day	Pyelonephritis and uraemia
	33	14th day	Pulmonary embolism
	35	Death on table	Cardiac arrest
B	57	62nd day	Uraemia secondary to clot retention and congestive cardiac failure
	9	Day of operation	Postoperative shock
	46	49th day	Toxaemia due to bed sores and bronchopneumonia
C	62	15th day	Pulmonary embolism
	21	27th day	Toxaemia secondary to carcinoma of bladder

TABLE V

Mortality

Grade of risk	Normotensive anaesthesia		Hypotensive anaesthesia	
	No. of patients	Deaths	No. of patients	Deaths
A	51	3	9	0
B	41	3	21	2
C	11	2	10	2
All cases	103	8	40	4

hypotensive anaesthesia; all cases were regarded as grade C risks. Bodman had a mortality of 4 per cent for his hypotensive series and 7 per cent for the control.

MORBIDITY

Tables VI and VII give the observed morbidity for the two series and table VIII compares it. It will be seen from table VI that in five cases, the changes recorded suggest an improvement rather than a deterioration in the patient's condition; these cases have been excluded from the comparison of morbidity.

No obvious difference in morbidity can be seen from table VIII.

The average time to discharge after the operation was 26.7 days for the normotensive series and 28.2 days for the hypotensive series. This suggests that the recovery was similar in both series and agrees with the findings of Bodman (1959) except that his hypotensive cases

TABLE VI

Morbidity in hypotensive series

Case No.	Blood urea mg per 100 ml		Serum bilirubin mg per 100 ml		Changes in teleradiogram pre-op.	Personality changes post op.	Other clinical morbidity post op.	Regarded as significant
	Pre-op.	Post op.	Pre-op.	Post op.				
8	46	36						
10	34	50						+
13	31	51						+
18						More irritable and depressed		+
20	58	40				Quieter and reads more	Phlebitis	+
21			2.1	1.1				
26	40	55	1.1	0.7				+
27	40	45			Moderate degree of cardiomegaly			+
28	50	44						
29			0.2	0.7				+
33	34	49						+
34	96	74						
37			0.4	0.2				

TABLE VII

Postoperative morbidity in the series of prostatectomies under normotensive anaesthesia

Grade of risk	Case No.	
A	74	Thrombophlebitis: Right leg (6th week)
	92	Phlebitis (10th day)
	29	Immediate postoperative collapse
	37	Pulmonary embolism (27th day)
B	78	Auricular fibrillation
	82	Clot retention (8th day)
	87	Cardiac failure and mental changes
	93	Cerebral embolism (14th day)
	97	Personality change—became excessively garrulous on 2nd day
	10	Oedema of both legs
	11	Cerebral haemorrhage (19th day)
	13	Auricular fibrillation (17th day)
	19	Clot retention
	38	Pulmonary embolism (12th day)
C	17	Immediate postoperative collapse with disorientation
	18	Severe reactionary haemorrhage and clot retention (8th day)
	43	Right basal pneumonia

TABLE VIII

Grade of risk	Normotensive anaesthesia		Hypotensive anaesthesia	
	No. of patients	Morbidity	No. of patients	Morbidity
A	51	4	9	2
B	41	10	21	4
C	11	3	10	2
All cases	103	17	40	8

TABLE IX
Reduction in the height of the P wave

Case No.	E.c.g. leads I	II	III	V5
4	Inferior nodal rhythm			
6	+	+	+	+
7	Nodal rhythm			
9		+	+	
14			+	
17		+	+	
18	+	+	+	
19		+	+	
22		+	+	
29	Nodal rhythm			
30	Inferior nodal rhythm			
38	Inferior nodal rhythm			

were on the average discharged slightly sooner than his normotensives.

ELECTROCARDIOGRAPHIC CHANGES

Our previous investigations (Rollason and Hough, 1959) had shown that it was dangerous to evaluate changes in the QRS complex using a single channel electrocardiograph and also that axis rotation very frequently recurred due to changes in the position of the heart. In the same study the PQ, QRS and QTC intervals did not appear to give useful information during hypotensive anaesthesia. Consequently, only changes in the P wave (table IX), ST segment (table X) and the T wave (table XI) were studied, and as in our previous work, minor changes were ignored. It was felt sufficient merely to record the sign of those changes which were deemed significant. Typical examples of the changes are illustrated in figures 1–3.

TABLE X
ST changes

Case No.	E.c.g. leads I	II	III	V5
1				+
4		+		
5	+			
7		+	+	
13	+	+		+
28				—
31		+		
32	+	+		+
35				—
36		+		
37		+	+	
38				—

+ = elevation — = depression

TABLE XI
T wave changes

Case No.	E.c.g. leads I	II	III	V5
1				+
2		—		—
3				+
4				+
5	+			+
6				+
7			+	—
9	—	—	—	—
10	+	+	+	+
13		+	+	+
14		—	—	
15		—	—	—
16				—
17				—
18				+
19		+	+	+
20	+	+	+	+
21		+		
23	+	+	+	+
24		—	—	—
27		+	+	+
28	•	•	•	•
29			+	—
30				+
32	+	+		+
35		—	—	—
36	+	+	+	+
37		+	+	
38		—	—	—
39	—	+	+	+
40	—		+	+

• = depression followed by elevation of T wave.
+ = elevation of T wave.
— = depression of T wave.

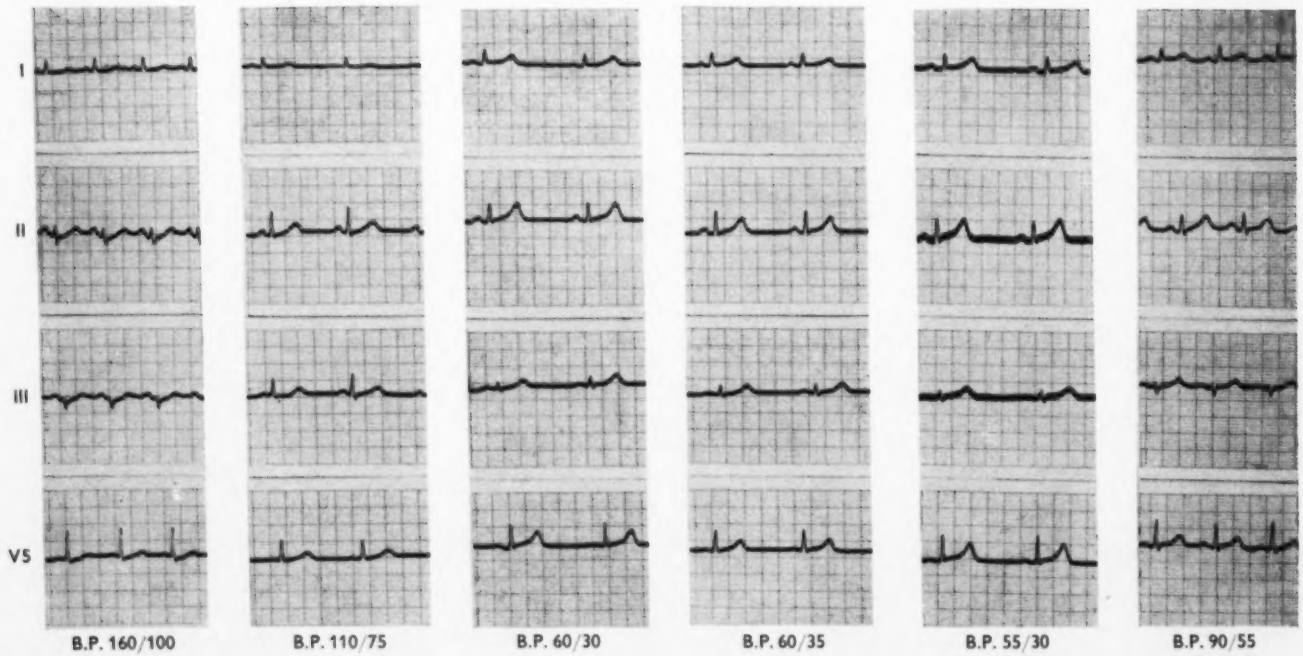


FIG. 1

Case No. 23. Serial electrocardiographs showing a reversible elevation of the T wave in all leads during the low pressure phase.

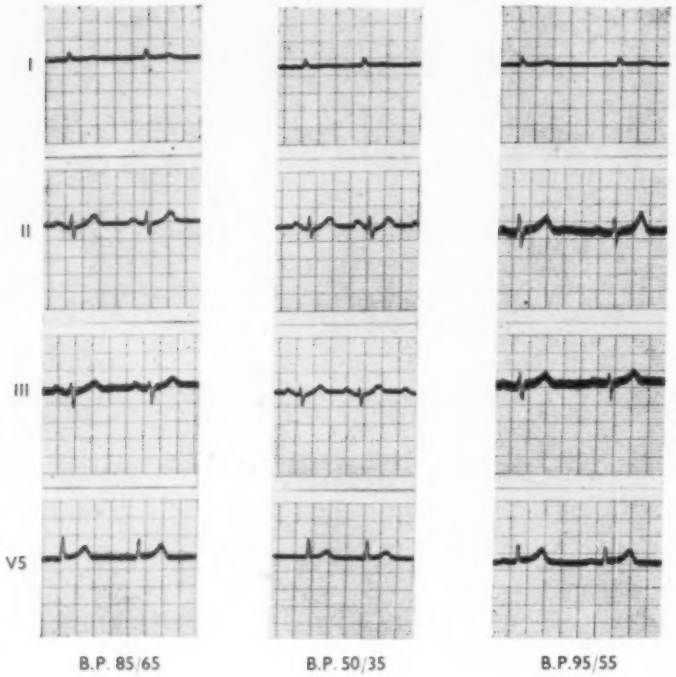


FIG. 2

Case No. 35. Serial electrocardiographs showing a reversible depression of the ST segment in lead V5 and of the T wave in all leads during the low pressure phase.

Attempts were made to correlate the e.c.g. changes with changes in pulse rate, hypotensive techniques and grades of risk, but no such correlation was found.

Age and blood pressures were two variables which could be factors in the production of e.c.g. changes. After some thought, the data is presented in the form of table XII. It will be seen that in the case of the T wave, only lead V5 has been used; the T wave was usually largest in this lead and the difficulty of changes in opposite directions in different leads was eliminated.

From table XII it will be seen that nodal rhythm and ST depression occurred more frequently in the oldest patients. The blood pressure during the hypotensive phase was markedly higher for those cases where no significant e.c.g. changes occurred; ST depression and nodal rhythm were associated with the lowest blood pressures.

An examination of the pre-operative blood pressures, shows that P wave changes and TV5 depression are associated with high pre-operative pulse pressure, whereas "no significant changes" occur with a low pre-operative pulse pressure.

It will be noted that the degree of hypotension produced was less marked in those with pre-operative blood pressures in the normal range. This was not a deliberate aim of the investigation but is probably associated with the fact that hypertensive patients are more susceptible to hypotensive techniques (Rollason and Hough, 1959).

A high pre-operative pulse pressure means that the patient has systolic hypertension, and there is a loss of elasticity in the great vessels.

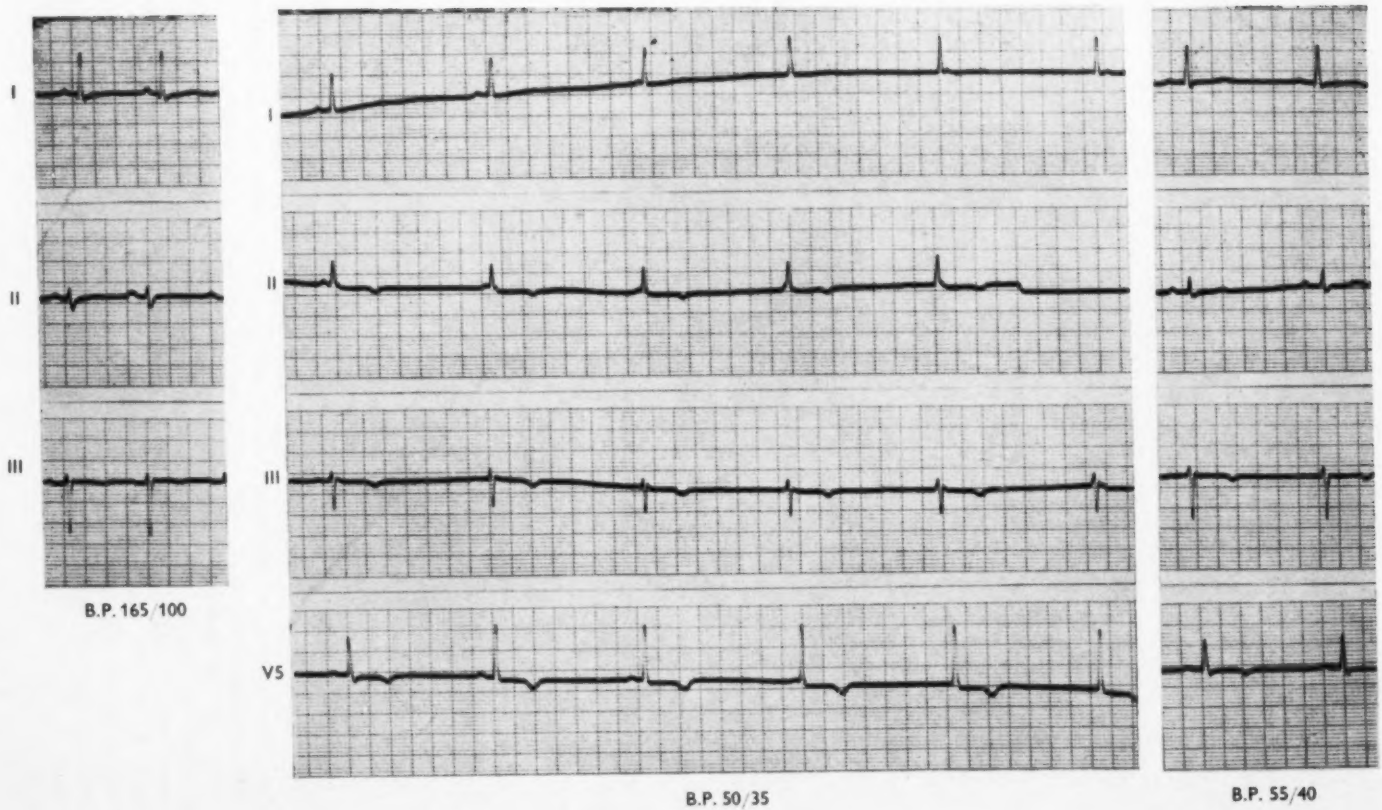


FIG. 3

Case No. 38. Serial electrocardiographs showing a reversible nodal rhythm together with a reversible depression of the ST segment in lead V5 and a tendency to T wave inversion.

TABLE XII

Summary of e.c.g. changes relative to age and blood pressure

				B.P. (mm Hg)		
		No.	Average age in years	Average pre-op. B.P. in mm Hg	Average pre-op. pulse pressure in mm Hg	Average lowest blood pressure in mm Hg
All patients		40	70.8	169/93	73	60/43
No clear change		6	72.2	147/83	62	79/57
P wave changes		12	71.1	178/95	82	55/39
Nodal rhythm		5	75.6	183/92	91	51/36
ST	Elevation	9	73.0	154/89	65	58/40
	Depression	3	79.0	167/93	73	50/32
TV5	Elevation	18	70.0	164/91	73	56/39
	Depression	10	72.0	187/105	84	58/42

It will be seen that this predisposes to P wave depression (including nodal rhythm) and reduction in the height of TV5. It might be expected that a reduction in the peripheral resistance caused by the hypotensive agent would produce a marked degree in the relative blood flow during systole and diastole. It is accordingly suggested that the systolic blood pressure should be kept at above 80 mm Hg in these cases.

Muster et al. (1950) showed that in cases of acute haemorrhage reversible myocardial insufficiency was associated with flattened or inverted T waves and ST segment depression. Many of the ST and TV5 elevations reported in this series have been in fact a tendency to eliminate an existing depression. At first sight, these might be regarded as suggesting an improvement in the oxygenation of the heart, but in fact Judson et al. (1956) suggest that such changes in their experience are indicative of myocardial ischaemia. It is concluded that in this age group a mild myocardial ischaemia of a readily reversible kind is likely to occur if the systolic blood pressure is reduced below 60 mm Hg.

From table I it will be seen that the pulse rate during the low pressure phase was usually not very different from the pre-operative value. With the exception of the patient who died, tachycardia was never observed. Inglis (1952) and Rollason and Hough (1959) have shown that a combination of tachycardia and hypotension is a warning that serious circulatory imbalance is likely to be present.

PATIENTS WITH A PREVIOUS HISTORY OF CEREBRAL AND CARDIAC INCIDENTS

In table II the six patients having a previous history of cardiovascular disease are examined. Only one death (No. 25) occurred among this group. One patient (No. 26) had an increase in blood urea but a decrease in serum bilirubin. Thus the mortality and morbidity were not clearly different from the other cases in this series.

The e.c.g. records are only available for five of these patients. No P wave changes were found, ST elevation occurred in two cases, and the T wave was elevated in two cases and reduced in one. Cases Nos. 8 and 26 were in the group "No significant change". Thus the e.c.g. changes observed are not different from those occurring in the whole group. It should be noted that the reduction in blood pressure was just as great for these patients as for the remainder of the series, and it appears possible that the hypotensive anaesthesia was in fact an assistance to their circulatory dynamics (Rollason and Hough, 1960).

CONCLUSIONS

Electrocardiographic changes suggestive of myocardial ischaemia were common at blood pressures of 60 mm Hg and below in the elderly.

Systolic hypertension predisposed to e.c.g. changes (particularly nodal rhythm or a lowering of the height of the P wave) during hypotensive anaesthesia.

The incidence of morbidity and mortality in the hypotensive series was not clearly different from that during normotensive anaesthesia.

A previous history of cardiovascular disease in these patients did not produce an increase in morbidity and mortality.

It is suggested that in patients of this age group the systolic blood pressure should not be allowed to fall below 60 mm Hg and that if a patient suffers from systolic hypertension the pressure should not be allowed to fall below 80 mm Hg.

SUMMARY

Morbidity, mortality and e.c.g. changes have been studied in a series of 40 cases undergoing retropubic prostatectomy under hypotensive anaesthesia. This incidence of morbidity and mortality was compared with that in a series of 103 cases undergoing the same operation with normotensive techniques and no important difference was found. E.c.g. changes suggestive of reversible myocardial ischaemia were frequently found when the systolic blood pressure fell below 60 mm Hg. Systolic hypertension predisposed the patient to e.c.g. changes. It is suggested that the systolic blood pressure should not be allowed to fall below 60 mm Hg in this age group and 80 mm Hg in the case of patients with systolic hypertension.

ACKNOWLEDGMENTS

Our thanks are due to Mr. J. R. Blackburn, F.R.C.S., and Mr. J. N. Young, F.R.C.S., for their co-operation, and to Mr. D. Patchett for technical help.

REFERENCES

Bodman, R. (1959). Blood loss during prostatectomy. *Brit. J. Anaesth.*, **31**, 484.

Debenham, L. S., and Ward, A. E. (1960). *Brit. J. Urol.* (in press).

Griffith, H. W. C. (1959). Personal communication.

Inglis, J. Mc.N. (1952). Management of hypotension during anaesthesia. *Lancet*, **2**, 362.

Judson, W. E., Hollander, W., and Wilkins, R. W. (1956). Observations on angina pectoris during drug treatment of hypertension. *Circulation*, **13**, 553.

Muster, A. M., Dack, S., Horn, H., Freidman, B. I., and Field, L. E. (1950). Acute coronary insufficiency due to acute haemorrhage; an analysis of 123 cases. *Circulation*, **1**, 1302.

Rollason, W. N., and Hough, J. M. (1959). Some electrocardiographic studies during hypotensive anaesthesia. *Brit. J. Anaesth.*, **31**, 66.

—— —— (1960). Is it safe to employ hypotensive anaesthesia in the elderly? *Anaesthesia*, **15**, 69. (Summary).

—— —— (1960). Is it safe to employ hypotensive anaesthesia in the elderly? *Brit. J. Anaesth.*, **32**, 286.

Brit. J. Anaesth. (1960), **32**, 286

IS IT SAFE TO EMPLOY HYPOTENSIVE ANAESTHESIA IN THE ELDERLY?

BY

W. N. ROLLASON

Royal Infirmary, Aberdeen, Scotland

AND

J. M. HOUGH

University of Hull, England

EVER since the introduction of induced hypotension, old age has been regarded as one of the factors against the employment of this technique. Cerebral or cardiovascular disease, and even old age alone, have been cited as absolute contra-indications (Enderby and Pelmore, 1951; Vandewater, 1953; Bedford, 1955; Gray, 1957; Haxholdt, et al., 1958). However, the work of Debenham and Ward (1960) who produced hypotension by using the combination of a "lytic cocktail" and spinal analgesia for retropubic prostatectomy with conspicuous success, stimulated us to reconsider the justification for these contra-indications. The reasons usually given are:

(i) the presence of atherosclerosis causing ischaemia of the vital organs at low pressure, and

(ii) the reduction in blood flow encouraging thrombus formation.

A search of the literature has shown that hypotensive techniques have been used in the elderly (i.e. in patients over 60 years of age) by many workers with reasonable success (Haxholdt et al., 1958; Davison, 1950; Camerini et al., 1952; Kilduff, 1954; Mandow et al., 1954; Cox, 1957; Pope, 1957; Gardner, 1958; Rollason and Hough, 1959. In these papers a total of 490 cases have been recorded with a gross mortality of 40, of which not more than 9 were associated with the anaesthetic technique used; not less than 16 had a previous history of cardiovascular disease. On the other hand, Mushin and others (1954) pointed out that in their experience postoperative complications were almost doubled in the 45–64 age group compared with younger patients when hypotension was employed.

The idea that age was a contra-indication to this technique originated during the period when the technique was being developed; at that time death occurred in all age groups due to a faulty understanding of the risks involved. Today the technique has found its proper use among younger patients and the advantages it presents to these would appear just as valuable to the aged if there is no sound physiological argument against its use. Its employment by Debenham and Ward (1960) during prostatectomy had enabled the use of an indwelling catheter postoperatively to be avoided with great benefit to patient and nursing staff alike.

The present investigation has been divided into two parts:

(i) a reappraisal of the evidence leading to the contra-indications to the technique, and

(ii) a study of a small number of cases of retropubic prostatectomy for signs of damage to the vital organs.

In reappraising the contra-indications, both physiological and pathological evidence on circulatory haemodynamics and also the results of the treatment of hypotension by hypotensive drugs have been studied.

CIRCULATORY HAEMODYNAMICS

The effect of changing blood pressure on the supply of blood to both the vital organs and the general circulation has received much attention in recent years. Burton (1954) introduced the important concept of a critical closing pressure below which vessels collapse; the magnitude of this pressure has not yet been clearly established, but the use of hypotensive anaesthesia with systolic blood pressures as low as 40 mm Hg has frequently been reported without mishap. Hence, it would appear that the only serious question is whether the vital organs are adequately oxygenated at these pressures.

Grayson (1952) has developed a technique of internal calorimetry and has employed this to study blood flow in the brain (Carlyle and Grayson, 1956), and liver (Grayson and Mendel, 1957) of various lightly anaesthetized animals. Provided the vessels were not cannulated he found that there was an "intrinsic regulation" of the blood supply, by which the blood flow rapidly returned to a constant value after a fall in blood pressure, and this value remained approximately constant down to systolic blood pressures of 40 mm Hg. For the brain, unlike the liver, the blood flow ceased abruptly at about 20 mm Hg. Shipley and Study (1951) have obtained similar results for the kidney.

Other investigations on the cerebral circulation are of interest. Bedford (1955) has pointed out that after an ordinary anaesthetic 7 per cent of a series of elderly patients showed signs of mental deterioration, which he presumed was caused by cerebral hypoxia. Clarke and others (1954) have reported a decrease in cerebral blood flow with increasing age or hypertension. At low blood pressures cerebral vascular resistance decreases and the arteriovenous oxygen difference increases in such a way that the circulation is adequate at systolic pressures of 50–60 mm Hg (Morris et al., 1953; Saunders, 1954; Van Bergen et al., 1954; Hughes, 1955) if the patient is supine and anaesthetized. Under thiopentone anaesthesia Kety (1949) has shown that cerebral oxygen consumption is reduced by 44 per cent. In conscious patients, however, below 60 mm Hg, there was evidence of some impairment of cerebral function, which is supported by the e.e.g. evidence obtained by Bromage (1953).

In the case of the liver, Bromage (1952) suggested that at pressures below 60 mm Hg local anoxia might be the cause of his observation that the liver became turgid and darkened, but this observation has not been confirmed by other investigators.

In the case of the kidney, renal function was found adequate down to pressures of 55 mm Hg (Morris et al., 1953; Miles et al., 1952; Evans and Enderby, 1952). This finding is supported by a case report (Mandow et al., 1954) where a patient was by accident kept at a systolic blood pressures of under 70 mm Hg for 36 hours. Gross mental changes ensued and two months later he died of anoxia and toxaemia caused by bed sores, but a postmortem examination yielded no evidence of renal damage.

The other vital organ is the heart and an inadequate oxygen supply will cause immediately obvious results. It has been shown (Eckenhoff, 1950; Little, 1957; Katz, 1958) that a fall in blood pressure produces a greater fall in cardiac work than in coronary flow, with the consequence that the heart is less likely to suffer from myocardial ischaemia during hypotension than at normal pressures.

To summarize, the evidence is that, in the healthy individual, with a systolic blood pressure in excess of 50–60 mm Hg, the oxygen supply to the vital organs is likely to be perfectly satisfactory during hypotensive anaesthesia in the supine position. The way in which this conclusion must be modified for the case of elderly individuals, particularly those with histories of cerebral or cardiac incidents or hypertension will be considered.

THE EFFECTS OF AGE ON THE CIRCULATION

In the elderly, besides the usual pathological disturbances of the circulation, some pathological conditions are so common that all must be suspected of possessing them to lesser or greater degree, even when clear clinical evidence is absent; they are atherosclerosis and the liability to thrombus formation in coronary and cerebral arteries. Hypertension is also common as a disease and not as a secondary consequence of some other primary disorder.

Elkeles (1957) has reviewed the relation between atheroma and coronary artery disease and has shown that it is unusual for a fatal occlusion to occur in markedly atheromatous portions of the vessels and that, in fact, calcified atheroma actually appears to offer protection against thrombus formation. Clearly sclerosed vessels will reduce circulation but such sclerosis, if at all general, would prevent a substantial reduction in blood pressure by the usual hypotensive techniques. Localized sclerosis will, of course, produce serious consequences for the sclerosed region. Beck (1958) has shown in dogs that it is localized myocardial anoxia which causes e.c.g. changes. This danger is probably reduced by the existence of a collateral circulation which appears

to become more effective with increasing age; the artificial development of such a collateral circulation is being studied by Day and Lillihei (1959) as a successful method of treating myocardial ischaemia.

Although atherosclerosis is often associated with hypertension, both can occur independently. Primary hypertension can be either due to loss of elasticity in the major vessels (systolic) or due to a more mysterious cause, probably of nervous origin (diastolic) (Pickering, 1955; Schroeder, 1957; Brod and Fencl, 1958). Systolic hypertension is characterized by a low diastolic pressure and a high pulse pressure, whereas diastolic hypertension has a high diastolic pressure and a more normal pulse pressure. In recent years it has been the practice to treat hypertensive individuals with ganglionic blocking drugs to maintain the blood pressure at a more normal level (Schroeder, 1957; Brod and Fencl, 1958). Such treatment differs in three respects from hypotensive anaesthesia:

The reduction in blood pressure is less.

The reduced pressure is maintained for prolonged periods.

The patient is conscious and leading a relatively normal life with greater cardiac loading than during anaesthesia.

Nevertheless, the experience of physicians in this field should be a valuable guide as to likely effects during anaesthesia.

Schroeder (1957) has pointed out that one danger of this treatment is that organic narrowing of arteries supplying the myocardium, brain, kidney and liver will cause ischaemia beyond the obstruction; however, in his experience it is fortunately rare to find such ischaemia in patients. A reduction of blood pressure in patients with angina associated with hypertension usually causes the angina to disappear, but in a few cases it may be aggravated (Schroeder, 1957; Turner, 1959; Doyle and Kilpatrick, 1954; Judson et al., 1956). Doyle and Kilpatrick (1954) have shown that in the majority of patients the coronary arteries are dilated rather than narrowed and that a reduction in pressure causes a greater fall in cardiac work than in coronary blood flow but that in the few cases where angina is made worse the reverse must be the case. These findings agree with the concepts put forward by Katz (1958) for the healthy heart. The fact that a moderate reduction of blood pressure can be maintained for years in these people with an improvement in their cardiovascular state suggests that a lowering of blood pressure is not likely to cause damage.

In the case of the brain, the evidence reviewed earlier suggests that in the anaesthetized patient a lowering of blood pressure is more likely to improve oxygenation than to reduce it, but clearly excessive sclerosis might invalidate this conclusion. It seems possible that Bedford's (1955) finding of an incidence of dementia in 7 per cent of the aged following normotensive anaesthesia, might not hold for hypotensive anaesthesia, but adequate evidence is not available on this point.

The main effect of a damaged kidney would appear to be a slower excretion rate for drugs circulating in the blood stream (Milne and Oleesky, 1951). and so a danger of prolonging unduly the period of hypotension.

In brief, it would appear that in the majority of indivduals, with hypertension, atherosclerosis or a history of coronary incidents, the reduced blood pressure is likely to improve the oxygenation of vital organs and so reduce the risk of ischaemia or infarction during an operation. In a small number of individuals, it would appear that the risk would be increased; clear evidence is not available to estimate in what percentage of cases this is true, but, on the bases of the medical treatment of hypertension, it must certainly be very small.

EXPERIMENTAL OBSERVATIONS DURING HYPOTENSIVE ANAESTHESIA

It seemed desirable to carry out a controlled investigation to discover whether, in fact, there was a serious risk in using hypotensive anaesthesia in the elderly. As Debenham and Ward (1960) had shown that a distinct surgical advantage (the avoidance of an indwelling catheter) arose from hypotensive anaesthesia for retropubic prostatectomy, this seemed an ideal operation to use for such an investigation. Our study of a series of 40 cases using hypotensive anaesthesia compared with a group of 103 cases where normotensive anaesthesia was employed, is reported elsewhere (Rollason and Hough, 1960). It is only necessary to summarize the main findings here; although the

emphasis was on e.c.g. changes during the low pressure phase, laboratory and clinical investigations were carried out to detect damage to the vital organs. There was no significant difference in terms of morbidity and mortalty between the group undergoing hypotensive anaesthesia and the group having normotensive anaesthesia.

E.c.g. changes occurred in 34 out of the 40 cases under hypotension; changes were most common in the P wave, the ST segment and the T wave. When the systolic blood pressure fell below 60 mm Hg the changes were more frequent. Nodal rhythm and P wave depression were common, the ST segment tended to be elevated and the TV5 showed both elevation and depression (ratio approximately 2:1). It is thought that both the ST and T wave changes may be due to a degree of myocardial ischaemia.

This investigation suggested that a reduction in systolic blood pressure below 60 mm Hg may produce a significant risk of myocardial ischaemia in the elderly. In fact half the cases investigated had a minimum systolic pressure below 60 mm Hg but their postoperative state was not significantly worse than the other half. If 60 mm Hg be regarded as the minimum safe systolic pressure, it would appear that damage to the heart is unlikely to occur except in that small group of patients with an organic narrowing of the arteries leading to a vital organ.

In the group of patients with systolic hypertension lowering of the height of the P wave (including nodal rhythm) and of the height of the T wave in lead V5 was common. This suggests that systolic hypertension predisposes to e.c.g. changes and to the risk of myocardial ischaemia. It is suggested that the systolic blood pressure should not be allowed to fall below 80 mm Hg in these cases.

In this series of cases the pulse rate usually decreased and even when it increased the change was small. It had been shown (Rollason and Hough, 1959) that a combination of hypotension and tachycardia was likely to be indicative of myocardial ischaemia.

THE EMPLOYMENT OF HYPOTENSIVE ANAESTHESIA

It has been shown that age is not an absolute contra-indication to this technique. It is now necessary to define the conditions under which it should be employed. The use of any method of anaesthesia must be justified in terms of the safety of the patient and on the improvement of the surgical conditions. A technique must be employed in the manner which yields the optimum advantages and minimizes its inherent risks.

The use of hypotension reduces for all age groups the capacity to respond to sudden emergency demands on the circulation; this means that the anaesthetist must always be vigilant. Skill is necessary on his part to provide a smooth anaesthesia with a perfect airway and adequate oxygenation. The blood volume must be maintained constant, and, prior to the operation, the haemoglobin content must be checked to see it is above 80 per cent (Vandewater, 1953). For the elderly, it is desirable to study the patient's record for previous coronary or cerebral incidents, and to examine the e.c.g. and e.e.g. pre-operatively. Wells (1953) however, has pointed out that coronary sclerosis may be advanced without clinical symptoms or e.c.g. evidence. During the operation, blood pressure and pulse rate should be checked frequently and a combination of tachycardia and low pressure calls for immediate action on the part of the anaesthetist.

Has hypotension sufficient advantages to justify its use in the elderly? The present work suggests that in many cases the patient may have a more satisfactory circulation at reduced pressures but the authors are forced to admit that in a small number of people the reverse will be the case. Further work on the problem seems to be called for to see whether it should not become almost routine to use hypotension in the elderly. At the present time it seems clear that its use is only justified when some surgical advantage ensues.

The reduction of blood loss is an advantage to the patient by avoiding the need for blood transfusion and to the surgeon by giving him a clear field in which to work. In the case of prostatectomy, the avoidance of an indwelling catheter is a major surgical advance which seems to justify the technique.

CONCLUSIONS

In the great majority of patients a reduction of blood pressure during anaesthesia is likely to assist oxygenation of the vital organs, but in a

small percentage of patients reduction in blood pressure will, in fact, cause a lack of oxygenation of the vital organs. At the present time, it is not possible to estimate the percentage accurately, but the evidence suggests it is indeed small and probably under 1 per cent.

Advanced atherosclerosis is not likely to encourage thrombus formation.

Our investigation suggests that ischaemia is unlikely to occur if the systolic blood pressure is above 60 mm Hg.

Systolic hypertension seems more likely to be associated with e.c.g. changes during hypotension than diastolic hypertension.

A previous history of coronary or cerebral incidents is not an absolute contra-indication to the technique.

Mortality and morbidity appear to be no greater with hypotensive than with normotensive techniques.

Hypotension should only be employed where the anaesthetist is both skilled and vigilant and where surgical advantages ensue from the technique. When it is employed the systolic blood pressure should not be allowed to fall below 60 mm Hg, or in the case of systolic hypertension below 80 mm Hg.

It is hoped to study a further series of cases under both e.c.g. and e.e.c. control in an endeavour to detect the small percentage of cases where the technique is definitely contra-indicated.

ACKNOWLEDGMENTS

Our thanks are due to Mr. J. R. Blackburne, F.R.C.S., and Mr. J. N. Young, F.R.C.S., for their co-operation, and to Mr. D. Patchett, for technical help.

REFERENCES

Beck, C. S. (1958). Applied physiology in relation to surgical operation for the treatment of coronary artery disease. *Circulation proceedings of the Harvey Tercentenary Congress*, 187. Oxford: Blackwell.

Bedford, P. D. (1955). Adverse cerebral effects of anaesthesia on old people. *Lancet*, **2**, 259.

Brod, J., and Fencl, V. (1958). Mechanism of general and renal hemodynamic diurnal changes. II: Behaviour of hypertensive subjects. *Čas. Lék. čes.*, **97**, 1025.

Bromage, P. R. (1952). Effect of induced vascular hypotension on liver; alterations in appearance and consistence. *Lancet*, **2**, 10.

—— (1953). Some electroencephalographic changes associated with induced vascular hypotension. *Proc. roy. soc. Med.*, **46**, 919.

Burton, A. C. (1954). Relation of structure to function of tissues of wall of blood vessels. *Physiol. Rev.*, **34**, 619.

Camerini, F., Gugliemi, F., and Pizzioli, R. (1952). Studio electrocardiografico nel corso di interventi operatori in ipotensione controllata. *G. ital. Anest.*, **18**, 503.

Carlyle, A., and Grayson, J. (1956). Factors involved in control of cerebral blood flow. *J. Physiol.*, **133**, 10.

Clarke, E., Hughes Jones, N. C., and Logothetopoulos, J. (1954). Action of tolazoline hydrochloride on cerebral blood flow in cerebral thrombosis. *Lancet*, **2**, 567.

Cox, R. (1957). Hypotensive anaesthesia. *Brit. J. Urol.*, **29**, 362.

Davison, M. H. A. (1950). Pentamethonium iodide in anaesthesia. *Lancet*, **1**, 252.

Day, S. B., and Lillehei, C. W. (1959). Experimental basis for new operation for coronary artery disease. *Surgery*, **45**, 487.

Debenham, L. S., and Ward, A. E. (1960). *Brit. J. Urol.* (in press).

Doyle, A. E., and Kilpatrick, J. A. (1954). Methonium compounds in angina of hypertension. *Lancet*, **1**, 905.

Eckenhoff, J. E. (1950). Physiology of coronary circulation. *Anesthesiology*, **11**, 168.

Elkeles, A. (1957). A comparative radiological study of calcified atheroma in males and females over 50 years of age. *Lancet*, **2**, 714.

Enderby, G. E. H., and Pelmore, J. F. (1951). Controlled hypotension and postural ischaemia to reduce bleeding in surgery; report of 250 cases. *Lancet*, **1**, 663.

Evans, B., and Enderby, G. E. H. (1952). Controlled hypotension and its effect on renal function. *Lancet*, **1**, 1045.

Gardner, E. K. (1958). Epidural analgesia for prostatectomy. *Anaesthesia*, **13**, 406.

Gray, T. C. (1957). Reflections on circulatory control. *Lancet*, **1**, 383.

Grayson, J. (1952). Internal calorimetry in determination of thermal conductivity and blood flow. *J. Physiol.*, **118**, 54.

—— Mendel, D. (1957). The role of the spleen and the hepatic artery in the regulation of liver blood flow. *J. Physiol.*, **136**, 60.

Haxholdt, B. F., Kjaer, K., and Secher, O. (1958). Controlled hypotension in maxillofacial surgery. *Acta anaesth. scand.*, **2**, 91.

Hughes, G. (1955). Investigation of cerebral blood flow during anaesthesia with hypotension induced by use of hexamethonium bromide and posture. *Brit. J. Anaesth.*, **27**, 229.

Judson, W. E., Hollander, W., and Wilkins, R. W. (1956). Observations on angina pectoris during drug treatment of hypertension. *Circulation*, **13**, 553.

Katz, L. N. (1958). The factors involved in the regulation of the heart's performance. *Circulation proceedings of the Harvey Tercentenary Congress*, 70. Oxford: Blackwell.

Kety, S. S. (1949). Physiology of human cerebral circulation. *Anesthesiology*, **10**, 610.

Kilduff, C. J. (1954). Use of arfonad in controlled hypotension. *Lancet*, **1**, 337.

Little, D. M. (1957). Induced hypotension. *Surg. Gynec. Obstet.*, **104**, 367.

Mandow, G. A., Arden, G. P., and Stoneham, F. J. R. (1954). Hypotension induced with hexamethonium bromide during anaesthesia. *Brit. J. Anaesth.*, **26**, 26.

Miles, B. E., de Wardener, H. E., Churchill-Davidson, H. C., and Wylie, W. D. (1952). Effect on renal circulation of pentamethonium bromide during anaesthesia. *Clin. Sci.*, **11**, 73.

Milne, G. E., and Oleesky, S. (1951). Excretion of methonium compounds. *Lancet*, **1**, 889.

Morris, G. C., Mayer, J. H., Snyder, H. B., and Haynes, B. W. (1953). Vascular dynamics in controlled hypotension: study of cerebral and renal hemodynamics and blood volume changes. *Ann. Surg.*, **138**, 706.

Mushin, W. W., Rendell-Baker, L., Lewis-Faning, E., and Morgan, J. H. (1954). Cardiff anaesthetic record system. *Brit. J. Anaesth.*, **26**, 298.

Pickering, G. W. (1955). *High Blood Pressures*. London: Churchill.

Pope, E. S. (1957). Halothane; a report on its use in twenty-five selected cases of pulmonary or cardiac disease. *Anaesthesia*, **12**, 405.

Rollason, W. N., and Hough, J. M. (1959). Some electrocardiographic studies during hypotensive anaesthesia. *Brit. J. Anaesth.*, **31**, 66.

—— —— (1960). Study of hypotensive anaesthesia in the elderly. *Brit. J. Anaesth.*, **32**, 276.

Saunders, J. W. (1954). Effect of controlled hypotension on cerebral function and circulation. *Lancet*, **1**, 1156.

Schroeder, H. A. (1957). *Mechanisms of Hypertension*. Springfield, Illinois: Charles C. Thomas.

Shipley, R. E., and Study, R. S. (1951). Changes in renal blood flow, extraction of inulin, glomerular filtration rate, tissue pressure and urine flow with acute alterations of renal artery blood pressure. *Amer. J. Physiol.*, **167**, 676.

Turner, R. W. D. (1959). Diagnosis and treatment of essential hypertension. *Lancet*, **1**, 897.

Van Bergen, F. H., Buckley, J. J., French, L. A., Dobkin, A. B., and Brown, I. A. (1954). Physiologic alterations associated with hexamethonium-induced hypotension. *Anesthesiology*, **15**, 507.

Vandewater, S. L. (1953). Morbidity, mortality and pathology in induced hypotension. *Canad. Anaesth. Soc. Proc.*, p. 62.

Wells, B. G. (1953). Electrocardiography during anaesthesia. *Anaesthesia*, **8**, 99.

Brit. J. Anaesth. (1960), **32**, 292

HIGH EXTRADURAL BLOCK FOR CERVICAL DYSTOCIA

BY

M. E. TUNSTALL

*The Middlesex Hospital, London, W.1**

IT is commonly believed that extradural analgesia for the relief of pain in labour or for the treatment of uterine inertia should not extend higher than the level of the tenth thoracic segment (Hingson and Hellman, 1956). Crawford (1959) repeats current teaching that extension upwards to the fourth or fifth thoracic segment will halt the progress of labour. Dawkins (1960) and Steel (1960) have subscribed to this view.

Johnson (1957) reported the results of a clinical trial of continuous caudal analgesia for prolonged labour. In his series there were twenty-three patients of whom three were refractory to treatment of 6 hours duration. In these three he continued analgesia for a further 6 hours to prove its inability to dilate the cervix. It is just in this kind of patient that it seems rational to try "uterine denervation" or high extradural blockade and the work of Alvarez, Poseiro and Pose (1959) supports this. They stated that in complete blockade of the nerve supply of the human uterus in labour, by means of subdural block, its tone as well as the frequency, intensity and duration of its contractions were completely unaffected. They also stated that, when uterine contractility was inco-ordinated, blockage of the spinal cord up to the sixth thoracic segmental level strikingly improved the pattern of uterine contractions in some cases.

The following report describes two cases of cervical dystocia who were treated by lumbar extradural analgesia. In both instances, after a period in which the two mothers were relieved of pain and recuperated their strength, but in which no progress in labour was made, the level of their sensory blockade was taken to a high level intentionally, so that as far as present knowledge goes, the uterus was totally cut off from the central nervous system. In both patients this appeared to lead to rapid dilatation of the cervix and delivery per vaginam when, prior to the extradural block, Caesarean section was a strong probability.

CASE 1

Age 27, para 0+0, E.D.D., 22.5.59.
Antenatal period uneventful.

20.5.59.

Time	
0001	Commenced labour.
1315	Admitted to the Middlesex Hospital. Vertex ROA. Head engaged. Contractions weak 1 in 15.
1845	Contractions good, 1 in 3.
1850	Pethidine 100 mg given.

21.5.59.

Time	
1830	Feels like pushing. Vaginal examination: vertex, mid-cavity, membranes intact, two fingers dilated, cervix soft but thickish. Contractions fairly good, 1 in 3–5. Pethidine 200 mg.
2200	"Getting into a state again."

22.5.59.

Time	
0025	Papaveretum 20 mg given.
1400	Vaginal examination: half-crown dilated, cervix thick anterior lip, membranes intact, head well applied to cervix, LOA. Urine acetone a trace. Contractions fairly good, 1 in 3–4.
1700	EXTRADURAL ANALGESIA.

Using the right paramedian oblique approach with a Tuohy needle a nylon extradural catheter was passed via interlaminar space between first and second lumbar vertebrae up to the level of the body of the twelfth thoracic vertebra in the extradural compartment. 1.5 ml of 1.5 per cent lignocaine was injected down the catheter followed 10 minutes later by 2.5 ml in the supine position. This completely abolished the pain of uterine contractions leaving perineal sensation unimpaired. Segmental block as ascertained by pinprick 20 minutes later extended from the twelfth thoracic to the second lumbar segment.

Time	
1945	Vaginal examination: three fingers, ant. lip + +. 3 ml 1.5 per cent lignocaine extradurally with patient propped up. This relieved all pain. Patient had only a sense of pressure in the pelvis with contractions.
2055	2 ml 1.5 per cent lignocaine extradurally. Pain relieved. Still wants to push down.
2150	Contractions good, 1 in 3–5. Quinalbarbitone sodium 200 mg.
2210	6 ml 1 in 600 cinchocaine extradurally.

23.5.59.

0005	Vaginal examination: no change.
0120	Mother distressed and wanting to push.

* Present appointment: Joint Senior Registrar, United Oxford and Portsmouth Group Hospitals.

Time
0140 5 ml 1 in 600 cinchocaine extradurally with patient sitting up.
0150 Pethidine 100 mg given.
0245 Resting well.
0330 Cinchocaine 5 ml repeated.
0500 Pethidine 100 mg given.
0630 Vaginal examination: cervix thinner but still three fingers dilated. Restless again, B.P. 140/80 mm Hg. Temperature 97.6°F. Pulse 120/min. Respiration 20 min. Urine showed a trace of albumin. F.H. 136. Contractions good, 1 in 4.
0640 5 ml cinchocaine extradurally, patient sitting up.
0830 Mother distressed. Contractions good, 1 in 5. Pethidine 100 mg given.
0900 HIGH EXTRADURAL BLOCK. 10 ml of 1 in 600 cinchocaine was injected rapidly down the extradural catheter with the patient supine and tilted 30° head down. Segmental block ascertained by pinprick extended from the seventh thoracic to the second lumbar segment. No hypotension developed and the patient was able to sit up 20 minutes later.
1015 Vaginal examination: cervix felt on left and anteriorly, thin and very well applied. Head midcavity.
1315 Repeat 10 ml cinchocaine as above.
1445 Block worn off. The patient was judged to be fully dilated and it was decided to allow the second stage to progress in the normal way.
1600 Vaginal examination: fully dilated, head low and midcavity. F.H. rapid.
1640 15 ml 1.5 per cent lignocaine given with the patient sitting up and a live baby girl (6 lb. 6 oz.) was delivered by forceps with the mother awake and co-operating at 1705 hours.

The total duration of labour was 89 hours, 5 min. Both mother and baby did well subsequently and the baby was breast fed.

CASE 2

Age 33, para 0+0, E.D.D. ? 22.6.59.

Antenatal period: B.P. 140/90 mm Hg from February onwards.

16.7.59.

Albumen in urine and patient admitted for induction.

17.7.59.

Time
0915 General anaesthetic. Head engaged. Vertex LOA. Cervix not dilated. One finger introduced with difficulty. Membranes swept. Hind waters ruptured and 2 oz. (60 ml) taken off. Foetal heart satisfactory.
1400 Enema and bath.

18.7.59.

2000 Backache. Butobarbitone 200 mg.

19.7.59.

0300 Contractions fairly good, 1 in 4.
0600 B.P. 150/90 mm Hg. Urine: albumen a trace.

20.7.59.

0230 Pethidine 100 mg.
0515 Patient rather distressed. Vaginal examination: cervix barely admits one finger, thick and feels rigid. Contractions good, 1 in 3–4.
0600 Patient very distressed. Pethidine 200 mg.
0900 Pethidine 100 mg.

Time
1200 Patient pushing. Vaginal examination: cervix thick, anterior fontanelle felt anteriorly. Contractions fairly good, 1 in 3–5.
1215 Morphine 15 mg. Scopolamine 0.4 mg.
1630 Vaginal examination: head low ROP, thick oedematous cervix 3–4 fingers dilated.

EXTRADURAL ANALGESIA

1730 Using the right paramedian oblique approach with a Tuohy needle a nylon extradural catheter was passed via second and third lumbar interlaminar space up to the level of the body of the first lumbar vertebra in the extradural compartment. 6 ml 1 per cent lignocaine was injected down the extradural catheter with the patient supine and in 20° head-up tilt. This relieved all pain except the rectal discomfort.
1740 6 ml 1 per cent lignocaine extradurally with the patient sitting up. Complete pain relief with the patient still aware of contractions.
1800 B.P. 145/90 mm Hg.
1840 7 ml 1 per cent lignocaine extradurally with the patient sitting up. Rectal discomfort relieved.
2020 Rectal discomfort returning. 10 ml 1 in 1200 cinchocaine extradurally sitting up. Block up to tenth thoracic segment (pinprick) but rectal discomfort not relieved satisfactorily.
2110 15 ml 1 in 1200 cinchocaine extradurally sitting up.
2130 Vaginal examination: head midcavity, cervix four fingers dilated, thick anteriorly and thin posteriorly.
2325 15 ml 1.5 per cent lignocaine extradurally, patient propped up.

21.7.59.

0405 Ditto.
0700 Contractions good, 1 in 10.
0745 20 ml 1.5 per cent lignocaine extradurally, patient propped up.
0850 Ditto.
1130 Vaginal examination: head low ROP cervix 3–4 fingers dilated. Outlet appears adequate.
1240 20 ml 1.5 per cent lignocaine extradurally, patient propped up.
1400 Ditto.

HIGH EXTRADURAL BLOCK

1430 20 ml 1.5 per cent lignocaine extradurally, patient supine and 20° head-down tilt. Subsequent block up to fourth thoracic segmental level (pinprick). (The B.P. rose from 140 to 150 mm Hg systolic.)
1545 Block wearing off.
1630 Strong contractions.
1715 Vaginal examination: fully dilated.
1850 50 ml 1.5 per cent lignocaine extradurally with the patient propped up. Forceps delivery with mother awake and co-operating. Live girl 7 lb. 3 oz. Both mother and baby did well subsequently and the baby was breast fed.

DISCUSSION

The pathway of uterine labour pain is via the eleventh and twelfth thoracic segmental levels. Sympathetic efferent nerves to the uterus are dissociated and arise from the sixth thoracic segmental level and below.

It seems that the uterus in labour does not wholly depend on nervous pathways to and from the central nervous system. The first stage of labour progresses normally after destruction of the spinal cord up to fourth thoracic segmental level (Dawson, 1943). Garrett (1959) believes that the large contractions of late labour and pregnancy appear to be secondary to the development of a physiological syncytial state within the uterine musculature. Embrey (1958) doubts the existence of a parasympathetic nerve supply to the uterus. The uterus is directly influenced by the sympathetic nervous system and Garrett (1954) concludes that pure l-adrenaline inhibits the large uterine contractions of late pregnancy and labour whereas pure l-noradrenaline stimulates them. He states also that inco-ordinate uterine action is probably associated with a derangement of the normal fine adjustments of the amounts of adrenaline and noradrenaline liberated at the nerve endings in the uterus.

As the uterus in labour can act without its nerve supply it is logical to try efferent sympathetic blockade in most cases of uncomplicated delay in the first stage. High extradural nerve block should be considered in those cases of uterine inertia which are not responding to blockade below the tenth thoracic segmental level. With a large number of cases to study it might be possible to formulate clear indications for this treatment and the scope of extradural analgesia in the treatment of uterine inertia might be widened.

The nylon or polyvinyl extradural catheter has greatly increased the safety and application of extradural nerve block. Such a catheter may remain in the extradural space for several days, for the purposes of prolonged analgesia, without ill effect. Using a differential segmental block a patient in the first stage may walk about pain-free with adequate proprioception and retaining the ability to micturate at will.

Extradural analgesia of the nature described requires the wholetime supervision of one who is deeply interested in the technique and has the requisite skill for its performance.

SUMMARY

Extradural blockade of the sympathetic efferent nerve supply to the uterus was performed in two cases. This was contrary to accepted practice and resulted in a dramatic full dilatation of the cervix.

A re-examination is suggested in the belief that extradural analgesia for the relief of pain in labour or the treatment of uterine inertia ought not to extend above the tenth thoracic segmental level.

ACKNOWLEDGMENT

I wish to thank Mr. Ian M. Jackson for permission to publish these two cases.

REFERENCES

Alvarez, H., Poseiro, J. J., and Pose, S. V. (1959). *11th International Congress of Physiological Sciences, Montevideo.*

Crawford, J. S. (1959). *Principles and Practice of Obstetric Anaesthesia,* 1st ed., p. 47. Oxford: Blackwell.

Dawkins, C. J. Massey (1960). Personal communication.

Dawson, J. B. (1943). Pregnancy and labour complicated by ascending myelitis and a bedsore of unusual size. *J. Obstet. Gynaec. Brit. Emp.,* **50**, 63.

Embrey, M. P. (1958). The effect of acetylcholine on the intact human uterus. *J. Obstet. Gynaec. Brit. Emp.,* **65**, 531.

Garrett, W. J. (1954). The effects of adrenaline and nor-adrenaline on the intact human uterus in late pregnancy and labour. *J. Obstet. Gynaec. Brit. Emp.,* **61**, 586.

—— (1959). A theory of uterine action. *J. Obstet. Gynaec. Brit. Emp.,* **66**, 927.

Hingson, R. A., and Hellman, L. M. (1956). *Anaesthesia for Obstetrics,* 1st ed., p. 135. Philadelphia, Montreal: Lippincott.

Johnson, G. T. (1957). Prolonged labour: a clinical trial of continuous caudal analgesia. *Brit. med. J.,* **2**, 386.

Steel, G. C. (1960). Personal communication.

CORRESPONDENCE

NEONATAL PHYSIOLOGY AND RESUSCITATION

Sir,—I would beg space to contest some of the views expressed in articles which have appeared in your recent pages—articles on the topics of neonatal physiology and resuscitation.

There can be no doubt that endotracheal intubation is an essential part of the scheme of neonatal resuscitation. I was most sorry to observe Professor Donald (*Brit. J. Anaesth.*, **32**, 106), and Dr. McDonald (*Brit. J. Anaesth.*, **32**, 22) continuing to pay at least lip service to "gastric oxygenation". This is a dangerous manoeuvre in the period immediately after delivery, because indulgence in it encourages the operator to delay passing an endotracheal tube. In such an event, the pulmonary tree fails to blossom out promptly, hence the pulmonary vascular tree is inadequately filled, and thus the normal changes in cardiovascular dynamics are retarded. The sequelae may include cardiac failure, regressive pulmonary efficiency syndrome (of which hyaline membrane disease may be the termination) and cerebral hypoxia.

Furthermore, "gastric oxygenation" is of no more worth than is playing oxygen through a nasal catheter or via a funnel placed over the mouth. In the Presbyterian Hospital, New York, last year, a group of which I was privileged to be a member was able to demonstrate that, certainly in newborn puppies, oxygen delivered into the stomach did not pass into the general circulation. This work is due to be published shortly. Actually we were merely repeating an investigation carried out several years ago at the same hospital by Drs. Virginia Apgar and Duncan A. Holaday, but I believe that that was not published either (contrary to popular belief, not all Americans are for ever rushing into print, just as not all British contributions are comprised of 10 per cent investigation and 90 per cent clinical impression).

Next I would like to chide Professor Donald for retaining those outworn terms "blue asphyxia" and "white asphyxia". They are fuzzy concepts of indefinite import. Definition and measurement are the bases of understanding, and only through understanding can rational treatment be applied. We must have a reasonably comprehensive system of criteria against which to measure the state of the neonate. Preferably this should be accepted on a national scale so as to facilitate the comparison of methods of conducting labour and delivery and of resuscitation. Once more I would urge that the Apgar scoring system (1953) be adopted—anyone can be taught it in 3 minutes—and I would suggest that the score be assessed at 1 minute and again at 5 minutes after delivery.

Professor Donald is also, I think, guilty of advocating the wrong narcotic antagonist. He virtually demonstrates this when he warns that "more harm than good will be committed unless nalorphine is used" only when a narcotic is known to be present in the child. Nalorphine, when given alone, will certainly cause respiratory depression. However, levallorphan (Lorfan) administered in the accepted dose range is far less likely to increase the degree of respiratory depression, should the latter, in fact, be of non-narcotic origin. Lorfan is undoubtedly the drug of choice in this context, though, of course, it is preferable that the mother should receive it with each dose of narcotic, rather than that its aid should be withheld until after delivery.

Regarding the limitations to be applied when giving I.P.P.R., I fear that Professor Donald is now somewhat out of date. The figures published by Day, Apgar and their colleagues in 1952 have now been superseded by those advised by Dr. Apgar and her group at the Sloane Hospital. I did attempt to communicate these facts recently (Crawford, 1959). A pressure within the range 25–35 cm H_2O, repetitively maintained for 0.5–1 sec, with an interval of about 1 sec between applications, will satisfactorily inflate the neonate lung. No machinery is needed—only the resuscitator's air- or oxygen-filled mouth.

Obviously the acceptance of this new finding will cause great relief, for who can with ease assess a period of 0.15 second?

I applaud Professor Donald's advocacy of the anti-Trendelenburg position for neonates after resuscitation and aspiration. It would have been better, I believe, had Dr. McDonald made it plain that the head-down tilt should be employed only until the upper air passages and the stomach have been cleared of potentially inhalable contents.

I have already contested several points made by Dr. McDonald in his article on Infant Physiology and Anaesthesia. I will forbear to comment on the details given regarding levels of oxygenation, or on the statement that "the foetus is accustomed to comparatively poor oxygenation at term". I would refer your readers to a recently published Symposium (Sissons and Whalen, 1960) and to a Review Article (James, 1959) for more reliably informative discussions on these questions.

Dr. McDonald states (p. 24): "The blood volume at birth is nearly 120 ml/kg of body weight, but this soon begins to fall and a normal value in a few months is about 90 ml/kg." As contributors to your later issue confirm (Graham, 1960; Anderson, 1960; Rees, 1960), the accepted figure at birth is about 85 ml/kg. Contrary to the concept of a rapid fall in volume, Sissons and Whalen (1960) have recently presented data by which they claim to show a startling rise in cell and plasma volume during the first few hours after delivery.

J. SELWYN CRAWFORD,

London, N.W.3

REFERENCES

Anderson, S. M. (1960). Premedication of children for surgery. *Brit. J. Anaesth.*, **32**, 126.

Apgar, V. (1953). Proposal for new method for evaluation of newborn infant. *Anaesth. and Analg.*, **32**, 260.

Crawford, J. S. (1959). *Principles and Practice of Obstetric Anaesthesia*, 1st ed., p.105. Oxford: Blackwell.

Day, R. L., Goodfellow, A. M., Apgar, Virginia, and Beck, G. J. (1952). Pressure-time relations in the safe correction of atelactasis in animal lungs. *Pediatrics*, **10**, 593.

Graham, G. R. (1960). Circulatory and respiratory physiology of infancy and childhood. *Brit. J. Anaesth.*, **32**, 103.

James, L. S. (1959). Physiology of respiration in newborn infants and in the respiratory distress syndrome. *Pediatrics*, **24**, 1069.

Rees, G. Jackson (1960). Paediatric anaesthesia. *Brit. J. Anaesth.*, **32**, 132.

Sissons, T. R. C., and Whalen, L. E. (1960). Blood volume of infants. III. *J. Pediat.*, **56**, 43.

Symposium (1959). *Oxygen Supply to the Human Foetus*. Oxford : Blackwell.

VAPORIZERS FOR HALOTHANE

Sir,—The paper by Baxter (1960) in the April issue of the Journal gives confirmation of facts which have been rumoured among anaesthetists for some time. Following his suggestion of the need for a simple halothane vaporizer, may I draw attention to the work of Burton (1958) on the use of the Rowbotham vaporizer for halothane.

Since then we have been using the new Goldman halothane vaporizer in a similar manner, and find it even more satisfactory. A full description of the use of this vaporizer is in the press, but may I state that provided the patient has spontaneous respiration it is impossible to get more than 3.5 per cent halothane in the circuit if there is a slight blow-off from the expiratory valve. This vaporizer has the added advantage of a graduated glass container for the halothane so that the actual volume of halothane being vaporized can be seen. And there is no increase in resistance to respiration with it in use.

F. R. GUSTERSON,

Worthing Group of Hospitals

REFERENCES

Baxter, V. T. (1960). Cardiac arrest following administration of a high concentration of halothane vapour. *Brit. J. Anaesth.*, **32**, 171.

Burton, P. J. C. (1958). Halothane concentrate from a Rowbotham's bottle in a circle absorption system. *Brit. J. Anaesth.*, **30**, 312.

Printed in Great Britain by JOHN SHERRATT & SON, Park Road, Altrincham

trophenium

REGD.

phenactropinium chloride

an agent for the production of controlled hypotension during general anaesthesia, providing ganglion blockade without direct vasodilator action. This original product of the Duncan Flockhart Research Laboratories is now available in the new, more convenient, pack of 20 ml. (1,000 mg.) in a box of 6 injection-type vials.

References: "The use of a homatropinium derivative to produce controlled hypotension" *Brit. J. Anaesth.* **29**, 342.

"Comparison of two hypotensive agents" *Anaesthesia*, **14**, 53.

"The use of Fluothane and Trophenium in anaesthesia for the surgery of deafness" *Scot. med. J.*, **3**, 496.

DUNCAN FLOCKHART OF EDINBURGH

The Doctors' House

Duncan, Flockhart & Co. Ltd., Edinburgh 11.

AST 274m

BRITISH JOURNAL OF ANAESTHESIA

VOLUME XXXII, No. 6 *Published monthly* JUNE 1960

Annual subscription (post free): Inland £3 15*s.*; *Overseas* £4 4*s.*; *U.S. and South Americas* $12.00

CONTENTS

PAGE

EDITORIAL 247

ORIGINAL

Studies with an Organic Buffer (T.H.A.M.) during Apnoeic Oxygenation in Dogs 248

By R. A. Miller, M.D., M.Sc., F.F.A.R.C.S., and G. F. Brindle, B.A., M.D., C.M., F.R.C.P.(C.), Department of Anaesthesia, Montreal Neurological Institute, and R. G. B. Gilbert, M.B., F.R.C.P.(C.), F.F.A.R.C.S., Department of Anaesthesia, McGill University, Montreal, P.Q., Canada.

Observations on a Rebreathing Technique for the determination of arterial P_{CO_2} in the Apnoeic Patient ... 256

M. K. Sykes, M.A., M.B., B.Ch., F.F.A.R.C.S., D.A., Department of Anaesthesia, Postgraduate Medical School, Ducane Road, London, England.

Halothane and Circulatory Occlusion. Some Experimental and Clinical Observations 262

G. R. Stirling, K. N. Morris, R. H. Orton, W. C. Boake, D. R. Race, Fay Kinross, J. W. Thompson, and W. Crosby, The Thomas Baker, Alice Baker and Eleanor Shaw Medical Research Institute, Alfred Hospital, Clinical Research Unit, Commercial Road, Prahran, S.1., Victoria, Melbourne, Australia.

PAGE

A Note on the Respiratory Effects of Anileridine 273

Mark Swerdlow, M.D., M.Sc., F.F.A.R.C.S., Department of Anaesthesia, Salford Royal Hospital, Manchester, England.

CLINICAL

A Study of Hypotensive Anaesthesia in the Elderly 276

W. N. Rollason, M.B., M.R.C.S., F.F.A.R.C.S., and J. M. Hough, M.A., The Royal Infirmary, Aberdeen, Scotland.

Is it safe to employ Hypotensive Anaesthesia in the Elderly? 286

W. N. Rollason, M.B., M.R.C.S., F.F.A.R.C.S., and J. M. Hough, M.A., The Royal Infirmary, Aberdeen, Scotland.

High Extradural Block for Cervical Dystocia 292

M. E. Tunstall, M.B., F.F.A.R.C.S., D.Obst.R.C.O.G., Queen Alexandra Hospital, Cosham, Portsmouth, Hants, England.

BOOK REVIEW 255

CORRESPONDENCE 295

JOHN SHERRATT & SON *Publishers* **PARK ROAD ALTRINCHAM ENGLAND**